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Cleveland Clinic Quarterly

A Bulletin Published by

The Staff of the Cleveland Clinic

CLEVELAND, OHIO

Vol. 6 JULY, 1939 No. 3

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CLEVELAND CLINIC QUARTERLY

Issued in four numbers during the year; one in January, one in April, one in July and one in October, by Cleveland Clinic Foundation, 2020 East 93rd Street, Cleveland, Ohio.

Entered as second-class matter March 4, 1935, at the Post Office at Cleveland, Ohio, under the Act of August 24, 1912.

THE FRANK E. BUNTS INSTITUTE

announces

A Course In

General Diagnosis and Treatment

on

MONDAY, TUESDAY, and WEDNESDAY
NOVEMBER 6, 7, and 8, 1939

and

A Course In

Diseases of the Eye, Ear, Nose, and Throat

on

MONDAY, TUESDAY, WEDNESDAY, THURSDAY, and FRIDAY
December 4, 5, 6, 7, and 8, 1939

Descriptions of these courses and outlines of the subjects to be covered will be published in the October, 1939 Quarterly.

THE USE OF LIVER AND IRON IN THE TREATMENT OF ANEMIA

RUSSELL L. HADEN, M.D.

Anemia is a reduction in the capacity of the blood to transport oxygen. Hemoglobin is the direct carrier of oxygen; the red cell acts as a container for the hemoglobin. In every anemia there is a decrease in hemoglobin; there may or may not be a reduction in the number of erythrocytes. The red cells are always altered, however, since the amount or concentration of hemoglobin in the cell must be abnormal, even if the number of erythrocytes is unchanged.

The total mass of red cells or erythron, which is best thought of as a vessel containing hemoglobin, is always changing. The normal erythron is kept at a constant volume, is made up of a constant number of red cells, and contains a constant amount of hemoglobin. In an adult male it has a volume of 2250 cc., contains nearly 800 grams of hemoglobin, and is made up of about 25 trillion red cells. The continuous alteration in the erythron is due to the fact that a red cell lives only about one month. When a cell dies, the stroma making up the framework disintegrates and hemoglobin is set free. The hemoglobin released is not used again as such but is broken up. Iron is split off, however, and a large part becomes a part of newly-made hemoglobin. It is possible the porphyrin nucleus of the disintegrated hemoglobin may be similarly employed. The stroma is not used again. Roughly, each day a trillion cells with a volume of 100 cc. and containing 30 grams of hemoglobin are destroyed so the same number must emerge from the bone marrow to keep the cell level constant. Nearly one billion red cells must be formed every minute of every day.

To make erythrocytes, water, mineral salts, protein, fat, and carbohydrate are required since the cells contain all these elements. Such nonspecific building materials are necessary to make all cells. To make the stroma of a normal red cell, at least one specific element is necessary. This is a chemical substance, the exact composition of which is unknown, formed by the action of a specific secretion of the gastric mucosa (the intrinsic factor of Castle) on some element in the food (the extrinsic factor of Castle). This substance is contained in liver and liver substitutes. It has the property of specifically maturing the cell or supplying the finishing touches in preparation for emergence from the bone marrow. This substance has been designated the erythrocyte-maturing factor (EMF).

As stroma is formed by nonspecific components and the specific erythrocyte-maturing factor, hemoglobin is deposited in the stroma to saturate it and make one-third of the final volume. The hemoglobin is elaborated by the reticulo-endothelial cells of the bone marrow. The

porphyrin nucleus needed for building the hemoglobin molecule seems abundant. One specific element, iron, is necessary for making hemoglobin. This is often deficient because the store of iron in the body is very small. To replace the 30 grams of hemoglobin normally destroyed each day, 100 mg. of iron are required. The total amount of iron in the body is roughly 4 grams and about 3 grams of this is in hemoglobin. Only about 85 to 90 per cent of the 100 mg. of iron set free from hemoglobin broken down each day is used again, so 10 to 15 mg. must be supplied daily to replace the deficit. The diet seldom contains much iron, so if there is a deficient intake of iron-containing foods an iron deficiency develops rapidly. When external hemorrhage occurs the most important loss is in iron. With internal hemorrhage the iron is conserved. A deficient iron intake or a loss of iron quickly causes a fall in hemoglobin.

With growth the total hemoglobin of the body increases since the blood constitutes a fixed fraction (about 1/13) of the body weight. If a normal man has 800 grams of hemoglobin, a child one-half his weight has only 400 grams of hemoglobin. As the total hemoglobin increases with growth, the store of iron in the body must become greater if properly supplied by food or medication. This growth factor is important in the anemia of younger individuals.

The formation of normal red cells containing the normal amount of hemoglobin is influenced also by conditions other than an adequate supply of the specific elements, the erythrocyte-maturing factor (EMF) and iron. Both specific factors are absorbed from the gastro-intestinal tract. With various abnormalities such as achlorhydria or diarrhea, absorption may be interfered with. Likewise, general conditions such as hypometabolism, infection, toxemia as from nephritis, or poisons, as lead, may interfere with normal marrow activity and so influence the building of red cells and hemoglobin. All such possible influencing factors must be taken into consideration in the use of liver and iron in the treatment of anemia.

In clinical anemia there may be a lack of the erythrocyte-maturing factor, of iron, or of both specific elements. This may be due to a deficiency in supply, absorption, or utilization, or result from increased need from growth, pregnancy, or increased metabolism.

An iron deficiency is the most common defect because of the small reserve supply of iron, the needs for growth, the relatively small amounts of iron in food, and the frequent loss of iron by chronic long-continued hemorrhage as from hemorrhoids or menorrhagia. An iron lack is detected by a decreased amount of hemoglobin per cell or low color index. At the onset of an iron deficiency the cells may be of normal volume but without the normal complement of hemoglobin as

shown by a low color index. If an iron deficiency continues the cells become smaller, seemingly because there is no use in having stroma if there is no hemoglobin to be carried. Every iron-deficiency anemia is thus hypochromic first and later microcytic as well as hypochromic.

Young, immature cells are larger than mature erythrocytes. As the cells mature with the incorporation of the erythrocyte-maturing principle, they become smaller. If there is a deficiency of the erythrocyte-maturing factor the cells are larger and the anemia is macrocytic and usually hyperchromic.

If there is a deficiency of both iron and the erythrocyte-maturing factor, the microcytosis of the iron deficiency may be cancelled by the macrocytosis of the EMF deficiency so a normocytic anemia may be the result of the deficiency of the two elements.

Iron and liver or liver substitutes for supplying the erythrocyte-maturing factor are indicated if there is a deficiency in supply or lack of absorption. In some cases where there is deficient utilization, an added supply may enable the bone marrow to take up more of the specific factor. Thus in chronic nephritis if the percentage of utilization of iron is lowered the anemia may be influenced by giving more although the supply may be adequate for normal utilization. Little is known about the actual amount of the erythrocyte-maturing factor used. In the hemolytic anemias with rapid regeneration of erythrocytes as shown by the high reticulocyte count, it is possible that the supply of erythrocyte-maturing factor is not adequate so added liver may be indicated to supply the excessive demand even if the production in the body of the specific principle remains constant.

The following facts concerning the physiology of the red cell have been emphasized:

1. Red cells and hemoglobin are constantly being lost and replaced.

2. The rate is very rapid as shown by a normal loss and replacement of a trillion cells and 30 grams of hemoglobin each day.

3. Specific and nonspecific elements are necessary for building red cells and hemoglobin.

4. The nonspecific elements are those required for making all cells.

5. The specific principles required are: (a) the erythrocyte-maturing factor (EMF) supplied by liver and liver substitutes to make the stroma of red cells and (b) iron for the synthesis of hemoglobin.

6. The erythrocyte-maturing factor is usually supplied to meet even abnormal demands as the liver and other organs contain a large reserve supply.

7. Added amounts may be required when: (a) a normal supply is not made in the stomach as in idiopathic pernicious anemia, (b) the

bone marrow cannot utilize the principle normally, and (c) when there is an excessive long-continued demand as in chronic hemolytic anemia where the production of new cells proceeds at an abnormally rapid speed to compensate for the cells lost.

8. The reserve store of iron is very small so an iron deficiency develops quickly if iron is lost through hemorrhage, or the intake is insufficient to meet normal needs.

9. Added iron is required to supply the (a) normal increased store that comes with growth, the physiologic increased need with pregnancy and lactation, and the loss of iron with menstruation, and (b) the deficit due to an inadequate intake, increased loss through hemorrhage, pathologic increased needs as in hyperthyroidism, decreased absorption as in achlorhydria, or impaired utilization by the marrow as in myxedema.

10. The need for liver is manifested by a macrocytosis of the red cells as shown by an increased volume index.

11. The need for iron is shown by a hypochromia of the red cells indicated by a low color index. With a long-continued iron deficit, a microcytosis is present also.

How may the erythrocyte-maturing factor be supplied? Glandular organs as the liver, kidney, and stomach all contain it. Liver and gastric mucosa are highest in specific content. Yeast also contains a significant amount. Where this principle is to be supplied, the inclusion of an adequate amount of protein and some liver in the diet should be insisted on. It is difficult, however, to get enough of the specific principle unless concentrates of liver and gastric mucosa are employed. The liver concentrates are the preparations of choice since these are available for both oral and parenteral use. Preparations of the gastric mucosa can be given by mouth only.

The parenteral use of the erythrocyte-maturing principle is the most efficient. The same amount of specific principle is 30 times as active with parenteral as with oral use. The efficiency of oral administration often decreases with age and continued use. Parenteral use is also more economical than oral administration when one considers the comparative amounts of specific principle necessary to bring the blood to normal and keep it so.

The ideal way to supply the specific maturing principle is to take a complete diet adequate in protein, fruits, and vegetables which includes a liberal serving of whole liver once or twice a week and to add to this liver extract parenterally.

Today, there are many liver extracts on the market. These have been increased greatly in potency and therapeutic effect. The better extracts are now standardized on the basis of units. One unit is the amount of effective principle needed each day to keep the blood normal.

Patients with idiopathic pernicious anemia vary greatly in the amount of principle required to return the blood to normal and to keep it at a normal level. The extracts can be standardized only on patients so one cannot be sure that a unit is always the same. A potent preparation of a responsible manufacturer only should be used. Even with such a preparation the best method of administration should be determined by each clinician. The concentrated extracts usually contain 15 units of the specific principle per cubic centimeter.

The most important use of liver extract is in the treatment of idiopathic pernicious anemia. This disease is most serious as is well shown by the fact that all patients suffering from the disease died before the advent of liver therapy. If undertreated, the patient may get along very well but continue to have a persistent, mild anemia. With undertreatment, however, a subacute combined sclerosis is very apt to develop and produce permanent crippling. It is much better to overtreat than to undertreat pernicious anemia, since the cost of liver extract is small as compared with the seriousness of the disease. Many different plans of treatment have been suggested. We have found the following plan very satisfactory over a number of years. When the patient first presents himself with active pernicious anemia or when in relapse, an injection of 1 cc. of a concentrated extract containing at least 15 units per cc. is given twice a week for the remainder of a 3 month period. For the second three months an injection is given once a week, and for the next six months one every two weeks. After this period of one year, usually only one injection each month is required although calculating from the unitage this is not sufficient. We have many patients who have gone as long as five years with the blood remaining normal under this plan of treatment. If the patient does not have a cord lesion when first seen, he should never develop one if efficiently treated. If there is already a cord lesion when treatment is begun, the treatment should be even more vigorous if the neurologic symptoms are marked. This may be carried out by continuing the frequent injections for a longer period, by giving liver oftener, and by adding liver extract orally.

The best criterion of efficient and complete therapy is the maintenance of a normal volume of the red cell. A complete blood study should be done at least every three months for the remainder of the life of the patient. An increase in the mean volume of the red cell always heralds a relapse or indicates incomplete therapy.

The manner of administration of liver extract in congenital hemolytic jaundice, in pregnancy, in sprue, and other conditions in which there is decreased absorption, increased need or impaired utilization must be determined by the severity of the need and treatment given accordingly. Here there is usually a macrocytosis of the red cells just as in pernicious anemia.

The question always arises concerning the value of liver in a frank hypochromic or iron deficiency anemia. With an achlorhydria there is always a possibility that liver extract may do good. With normal gastric acidity it is very unlikely that the liver extract will influence the anemia.

A hypochromia with or without a microcytosis indicates that the stroma of the cell is not sufficiently supplied with hemoglobin. This deficiency is due to a defect in supply of iron to the bone marrow or a lack of utilization of iron in the marrow. If the hypochromia is due to defective utilization of the iron from chronic nephritis, malignancy, infection, or hypothyroidism, the anemia may be helped by giving large amounts of iron since the total amount utilized is increased although the percentage may be unchanged.

If the hypochromia is due to a deficient supply of iron by reason of deficient intake, or by reason of an increased iron loss due to hemorrhage, the effect of giving iron is usually rapid and complete if the proper preparation of iron is taken.

What preparation of iron should be employed? Iron is present in the hemoglobin molecule in the ferrous form. All the evidence indicates that iron given in the reduced state must be oxidized to the ferrous form and if given as a ferric salt must be reduced to the ferrous state. Almost any iron preparation is potent if given in large enough amounts, but smaller amounts of the ferrous salts are required than of reduced iron or ferric salts. The best preparations are ferrous carbonate, ferrous chloride, and ferrous sulphate. These are all cheap and efficient. The relative utilization of the different medicinal preparations is given as follows by Witts:

Preparation	*Effective Daily Dose Grains*	*Iron Content Mg.*	*Utilization of Iron Per Cent*
Metallic:			
Reduced iron	20-90	1200-1500	0.5-2
Ferrous:			
Ferrous chloride	4-8	100-200	12.5-25
Ferrous sulphate	9-12	180-240	14.0
Ferrous carbonate (As Blaud's pills)	45-60	300-400	8.0
Ferric:			
Ferric ammonium citrate	60-120	800-1600	1.5-3

It is evident from these data that reduced iron and ferric salts should never be given if ferrous preparations are available. Ferrous sulphate should be given in doses of 9 to 18 grains daily. Smaller amounts of

ferrous chloride are required (9 to 12 grains). The chloride is best given in a 5 per cent solution in a mixture of 3 parts water and 1 part simple syrup. I have long used a pill containing 2 4/5 gr. ferrous sulphate and 1 4/5 gr. sodium carbonate. Six tablets are given daily. Blaud pointed out over one hundred years ago that this is a most efficient preparation. In my hands it has been the most satisfactory of all preparations.

The oral preparations of iron are so efficient there seems little reason for using parenteral iron therapy. It is true that iron given parenterally is 30 times as active as when given by mouth but the margin between effective and toxic doses is small. Utilization is good by mouth and ferrous salts are very cheap.

With the administration of an active iron preparation in optimum amounts the hemoglobin will increase 1 to 2 per cent each day. If the fault is due to poor utilization, the rise is much smaller unless the cause for the poor utilization is corrected, as by giving thyroid extract in myxedema. If the cells are small to begin with, they get larger as iron is supplied to make hemoglobin. If the cause for the iron deficiency such as hemorrhoids is corrected after the hemoglobin returns to normal, iron medication does not need to be continued. In certain cases, as in idiopathic hypochromic anemia where absorption seems impaired, it is best to continue iron one week of each month. This method seems to keep the supply up to normal.

Should other metallic elements, such as copper, be given with iron? In adults, at least, there is little evidence that added copper is of value. All medicinal iron preparations contain some copper, so if any is needed this should be enough. In the same way there seems no reason for adding vitamin B to complement or supplement iron.

Should iron and liver therapy be given together? If the erythrocyte-maturing principle is needed, iron is seldom lacking. If iron is indicated, the anemia is seldom influenced by liver extract. Only rarely does an iron deficiency occur with a deficiency in the specific principle of liver. If there is an achlorhydria with the hypochromia the effect of liver may be tried. Cases of a combined deficiency, however, are rare. The important thing in every anemia is to determine the need and supply this effectively. There is no point in wasting money on liver extract if no deficiency in the specific maturing principle exists; iron should not be given if there is no lack of iron.

Summary

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Summary

1. The physiology of the red cell has been reviewed and the factors influencing the supply and use of iron and the specific principle of liver emphasized.

2. The erythrocyte-maturing principle is best supplied as liver extract administered parenterally.

3. When the specific principle is needed, as in pernicious anemia, an adequate amount of a potent extract must be given.

4. Pernicious anemia should be overtreated rather than undertreated.

5. With complete therapy the macrocytosis characteristic of a deficiency in the erythrocyte-maturing factor should disappear.

6. Iron should be given in the ferrous form and in adequate dosage.

7. There is seldom an indication for parenteral iron therapy.

8. With correct therapy the hypochromia and microcytosis characteristic of an iron deficiency should disappear.

9. Both liver extract and iron are seldom needed. Liver extract should be given in a hypochromic anemia only if an achlorhydria is present.

10. Careful attention should be given to correcting factors which unfavorably influence the absorption and utilization of the specific factors.

BILATERAL SIMULTANEOUS URETEROSIGMOIDOSTOMY FOR CHRONIC INTERSTITIAL CYSTITIS

Report of a Case

WILLIAM E. LOWER, M.D., and F. C. SCHLUMBERGER, M.D.

Transplantation of the ureters into the rectosigmoid is now a recognized procedure in the treatment of various types of intractable lesions of the bladder. Its success has been proved in the treatment of exstrophy of the bladder and, if no complications exist in the upper urinary tract, it may be performed with a relatively low mortality. In carcinoma of the bladder, circumstances often exist which render such an operation more hazardous. Obstruction and infection in the upper urinary tract is more often encountered in such cases. In irremediable vesicovaginal fistulae which have not lent themselves to the usual methods of surgical correction and also in cases of extensive chronic interstitial cystitis, interference with the structure and function of the upper urinary tract occurs less frequently. Consequently, ureteral transplantation is more applicable in these cases.

We wish to present the case of a patient who was disabled with extensive chronic interstitial cystitis. In this instance a bilateral ureterosigmoidostomy was done, both ureters being placed in the rectosigmoid at the same operation.

REPORT OF CASE

A housewife, 53 years of age, came to the Clinic on March 3, 1939, complaining of severe dysuria, frequency, nocturia, and suprapubic distress; these symptoms had been present for ten years. The initial symptoms had been frequency and mild dysuria. However, she soon began to have some nocturia and noticed that a very small amount of urine was passed at each voiding. The urine was always very clear. A uterine suspension was recommended and carried out elsewhere but this did not add to her comfort. A course of roentgen therapy was given but was of no avail.

The symptoms became increasing more severe. Constant urgency developed and the patient experienced diurnal frequency every half hour and nocturnal frequency equally as often. She finally resorted to the oral administration of morphine sulfate to obtain relief. In 1937 it became necessary for her to take as much as 38 or 40 grains of morphine each week.

Early in 1937, after eight years of suffering, she consulted a urologist and a diagnosis of chronic interstitial cystitis was made. The usual forms of treatment were instituted. When first undertaken, fulguration of the involved areas gave relief for about three months. Over a period

of two years, nine fulgurations were done and little result was obtained from the last two. During this time it was necessary for her to take 10 to 12 grains of morphine each week.

It was at this time that the patient was referred to the Clinic to accept any form of treatment which might afford some permanent relief.

Physical Examination: Nothing outstanding was found on physical examination. The temperature was 98.6° F., pulse rate 72 beats per minute, blood pressure 130 systolic and 80 diastolic. There was a midline scar in the lower part of the abdomen and some tenderness over the lower abdomen.

Laboratory Procedures: Examination of the blood showed 4,600,000 red cells, 71 per cent hemoglobin, and 5,750 white cells. The level of the blood sugar was 96 mg. and of the blood urea 36 mg. per 100 cc. The blood Wassermann and Kahn tests gave negative reactions. Urinalysis showed the pH to be 6.0, no albumin or sugar was present; an occasional white blood cell and a few red blood cells were found. Culture of urine from the bladder proved to be sterile.

Roentgen study of the upper urinary tract indicated no pathologic lesion. Intravenous pyelography showed both kidneys to have prompt and good function; there was no ureteral dilatation or evidence of ascending infection.

The patient was admitted to the hospital. A *cystoscopic examination* was carried out under spinal anesthesia. The bladder capacity was found to be very small, approximately 50 cc. The entire bladder was diffusely inflamed and there were extensive areas of ulceration. There were no encrustations. Both ureteral orifices appeared quite normal. Upon distending the bladder there was generalized capillary oozing. The cystoscopic picture was characteristic of extensive chronic interstitial cystitis with ulceration. It was our opinion that diverting the urinary stream was the best method of treatment which might afford her some relief.

The usual cleansing routine in preparation for a colonic operation was instituted. Briefly the routine consists of a diet of non-residue food with additional glucose candies. Saline cathartics are administered each morning for two days, with cleansing enemas in the evening. On the third day the bowel is placed at complete rest.

On the fourth hospital day both ureters were transplanted into the pelvic portion of the colon, the left being transplanted first. A suitable site was selected at a point approximately at the junction of the sigmoid and rectum. A ureteral bed between the muscularis and mucosa of the bowel was prepared for a distance of two inches. The ureter was fixed

into the bed and its end tucked through a small opening in the mucosa into the lumen of the bowel at the distal end of the ureteral bed.

A similar procedure was carried out on the right side. However, the site of implantation on this side was some distance below that on the left. The abdomen was closed without drainage and a tube was placed in the rectum. The patient withstood the operative procedure well.

Catheters or splints in the ureters were not used. If the implantation is carefully done and care is taken not to draw the sutures too tight, the urinary flow is adequate the first few days following the anastomosis.

The quantity of urine secreted on the first day was 1125 cc. On the second day there were 1910 cc., on the third day 1590 cc., and on the fourth day 1450 cc. Drainage of urine continued very favorably and on the eighth day 2475 cc. were secreted. The rectal tube was removed on the ninth postoperative day.

The highest temperature reading recorded, 102.4° F., occurred on the first postoperative day (Chart 1). At no time was there any radical

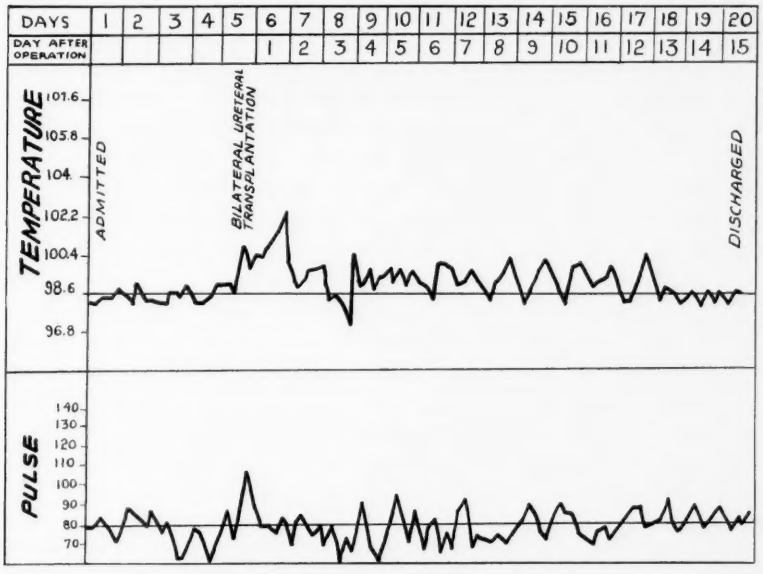

CHART 1: Chart showing temperature and pulse curves.

change in the blood chemistry. The blood urea determination was never more than 42 mg. per 100 cc.

When the patient was discharged from the hospital on the fifteenth postoperative day, she had complete symptomatic relief and required no narcotics.

The last observation of this patient was made two months following

operation, at which time she had gained 12 pounds in weight and had been perfectly comfortable.

Chronic interstitial cystitis is one of the most persistently distressing conditions which involve the urinary bladder. Only a small portion of the bladder may be involved; if so, these regions may be treated by lavage, medical agents, cautery, and finally overdistension. However, when large portions of the bladder become affected, it is almost impossible to control the condition by such methods. When of long standing, this disease produces a small, contracted, rigid bladder with a capacity of only a few ounces. The result is extreme pain and great disability as was truly demonstrated in this case. In this state, life becomes intolerable, the patients are social outcasts, and diversion of the urinary stream is the only procedure which offers comfort to the patient. The question then is one of rehabilitation from an unendurable state to one of comfortable existence with a minimal surgical risk. In order to accomplish this, several factors must be considered.

1. What is the general physical condition of the patient? Have abdominal operations been performed previously which may make the procedure more hazardous?

2. What is the condition of the upper part of the urinary tract? Fortunately, in cases of chronic interstitial cystitis the disease usually remains confined to the bladder. Sometimes it is complicated by the formation of encrustations which may produce obstruction.

3. Proper preparation before operation has proved itself very essential both as an aid in carrying out the surgical procedure and in bringing about a favorable outcome.

4. Careful selection of the position in the bowel for implantation of the ureters is of prime importance. That position which allows the ureters to lie in their most natural positions, without becoming tortuous or kinked, is the one to be used.

5. Careful attention must be given to details during the postoperative period with special reference to the maintenance of adequate fluid intake and urinary output.

Whether one ureter should be transplanted at a time or both transplanted simultaneously is a moot question. In the patient who is a poor operative risk, the hazard of the operation may be increased if both ureters are transplanted at once. It has been our experience that the reaction following implantation of the second ureter is as great as that following the first. A number of simultaneous bilateral transplantations of the ureters have been performed at this Clinic. We are of the opinion that in patients with general good health and with the improved preoperative preparation and surgical methods, bilateral simultaneous ureteral transplantations may be utilized more frequently.

THE INDICATIONS FOR DUODENAL DRAINAGE: ITS RELATION TO CHOLECYSTOGRAPHY

E. N. COLLINS, M.D.

Since its clinical application by Lyon in 1919[1], the Meltzer-Lyon method of duodenal drainage has proved physiologically sound but its clinical value has been disputed. When cholecystography was introduced by Graham and his coworkers in 1924[2], interest in this procedure diverted attention from duodenal drainage for a number of years. During the past 14 years, however, the value and limitations of cholecystography have become established. Due to certain limitations of cholecystography, duodenal drainage is again being used by an increasing number of clinicians in conjunction with cholecystography and other roentgen examinations, each procedure giving findings complementary to the other.

In our experience cholecystography has proved the most important single diagnostic procedure pertaining to the biliary tract. The use of newer developments in technic[3,4,5] has enhanced its accuracy. However, there are instances in which the gallbladder has been removed, where jaundice of a sufficient degree to contraindicate the use of cholecystography exists, and when both clinical and cholecystographic findings are indeterminate.

Although we do not use duodenal drainage routinely in the investigation of the upper gastro-intestinal tract, in recent years it has been employed in an increasing number of cases and it has given important information which could be obtained in no other way.

In this communication certain features relative to an appraisal of both cholecystography and duodenal drainage will be mentioned, and the indications for duodenal drainage, according to our experience, will be presented.

In attempting to relax the sphincter of Oddi and promote drainage of bile, it should be recalled that the administration of magnesium sulfate and other gallbladder stimulants *by mouth* produce a result different from that obtained by introducing the substance directly into the duodenum (Fig. 1). Not only is hypertonic magnesium sulfate reduced to isotonicity in the stomach but at least a part of the solution is converted into magnesium chloride, and when it reaches the duodenum the union with sodium results in its conversion to sodium sulfate. Physiologists have reported that sodium sulfate tends to constrict instead of relax involuntary muscle.

The increasing interest in the study of the "post-cholecystectomy syndrome" has again emphasized the importance of earlier diagnoses in

FIGURE 1a: Roentgenogram showing a normally functioning gallbladder by cholecystography during the course of duodenal drainage.

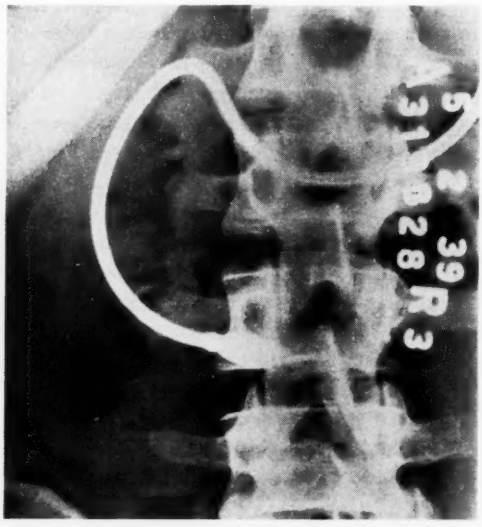

FIGURE 1b: Roentgenogram showing complete emptying of the gallbladder one hour after the injection of hypertonic magnesium sulfate into the duodenal tube.

order to prevent the late sequelae of biliary disease. We believe the medical profession has not realized the significance of the published findings of the clinicians who have had considerable experience in the use of duodenal drainage. These clinicians have found that duodenal drainage has given earlier evidence of abnormality in the biliary tract than has been obtained by other diagnostic means. The increasing use of this procedure, both preoperatively and postoperatively, indicates that its value is becoming more widely recognized. Bockus, Shay, Willard, and Pessel[6] have shown that, in their experience, "bile drainage has proved superior to cholecystography in gall stone diagnosis." Allen O. Whipple[7], in presenting a study of 700 unselected, consecutive patients having biliary or pancreatic lesions operated upon by himself during the 20 year period from 1914 to 1934, states, "The findings of cholesterol crystals, calcium bilirubin particles, and pus cells with bacteria in the duodenal contents obtained by duodenal intubation is, in our experience, even more reliable than cholecystography in demonstrating true pathology; that is, a lesion requiring surgical therapy." An interesting sidelight on the question of duodenal drainage was made by one of our urologists after the subject was discussed at a Staff Meeting. He said, "It seems to me that a diagnosis of significant biliary disease could not be made without knowing the findings on duodenal drainage any more than I could make a diagnosis of significant urinary tract disease without urinalysis." In view of investigations pertaining to the formation of renal and biliary calculi and infections in the urinary and biliary tracts, this comment was not without significance.

Certain limitations relative to cholecystographic procedures have not received sufficient emphasis; for example, normal cholecystographic findings do not exclude the presence of a significant cholecystitis. We must recall the fact that a gallbladder full of calcium-type gall stones often functions normally, as determined by cholecystography and, in this instance, a diagnosis of chronic cholecystitis, as well as cholelithiasis, is usually made in spite of the normal function.

Except in unusually acute conditions, surgeons have learned to place considerable reliance on the cholecystographic findings before advising surgical procedures. Although there has been considerable controversy relative to the significance of the so-called "innocent gall stone," all are agreed that the best results from surgery of the gallbladder are obtained in those patients who have had definite biliary colic. The relatively huge number of patients having cholecystography as compared with the small number having operations has not received sufficient recognition. Relatively few patients having normal cholecystographic findings have operations on the biliary tract. Those

having non-visualization of the gallbladder by cholecystography without evidence of opaque calculi rarely have operations unless there is a history characteristic of biliary colic. Therefore, the cholecystographic findings are not checked by the surgeon and pathologist in these instances.

If we are to make an *early diagnosis* of significant biliary disease, prevent the late sequelae of this condition, use the established newer developments in medical management, particularly as it pertains to metabolic disturbances, the infectious factors, and stasis, we believe the more widespread use of duodenal drainage, particularly in borderline cases, proves important.

Indications for Duodenal Drainage

A. *Diagnosis*

1. Suspected biliary disease; gallbladder has been removed
   Post-cholecystectomy syndrome
   a. Suspected common-duct stone
      Chronic cholangitis
   b. Stricture of common duct
      Is bile obtained by duodenal drainage?
      Time of onset of jaundice after cholecystectomy
      Is jaundice increasing progressively?
   c. Spasm of sphincter of Oddi; biliary dyssynergia
2. Presence of jaundice
   History and physical findings indeterminate
   No opaque stones visualized by roentgen examination
   Character of bile, if obtained
   Is icterus index curve rising or falling?
3. Absence of jaundice
   a. History characteristic of biliary colic
      Cholecystographic and other roentgen findings normal
   b. Suspected biliary disease; history and physical findings indeterminate; other causes for patient's symptoms excluded
      1. Normal cholecystographic findings
      2. Non-visualization of the gallbladder by cholecystography and no opaque stones visualized
4. Suspected pancreatic disease
   Is purulent material or other inflammatory products obtained?
   Pancreatic enzymes
   Character of bile, if obtained
5. Certain diseases of the liver, such as biliary cirrhosis
6. Postoperative appraisal of state of biliary tract

B. *Treatment*

Pancreatitis; "Catarrhal" jaundice (shortens course);

Non-calculous biliary tract disease, if other indicated measures of treatment prove inadequate. Intractable urticaria; the use of a vaccine made from cultures of bile obtained by duodenal drainage has proved effective in the treatment of intractable urticaria when other procedures from the standpoints of allergy and gastro-intestinal function prove ineffective.

Significant Findings—Duodenal Drainage

1. Absence of concentrated bile
   (Gallbladder present)
   Repeated stimulations; possibly repeated on separate days;
   Correlation with roentgen findings
   Consider abnormal function of gallbladder, cystic duct obstruction or gallbladder containing stones; psychic factors.

2. Presence of
   a. Cholesterol crystals
   b. Calcium bilirubinate pigment
      1. If jaundice is not present
         presence of both (a) and (b) usually indicates gall stones, cholesterosis, or pre-calculous state
      2. If jaundice is present or has been present recently
         presence of (b) alone is not significant
         presence of (a) alone may indicate cholesterosis
         presence of both: as indicated in (1)

Suggestive Findings—Duodenal Drainage

1. Unusual number of bile-stained pus cells
2. Abnormal cell exfoliation
3. Bacterial clumps—number and amount in concentrated or last bile fractions
4. Bacteriological examination

Technic

The value of duodenal drainage depends to a great extent on the care and exactness of the technic used, as well as the experience of the examiner. Although these criteria are always employed in judging the value of cholecystography and other laboratory procedures, they may not be given equal emphasis in the appraisal of duodenal drainage. This communication is based on the work done or supervised by a technician who has had ample training and experience with Doctors Lyon and Bockus. Because of its proved value in producing contraction of the gallbladder during cholecystography, an egg-yolk-lecithin-glycerine mixture[5,8] has been injected through the duodenal tube when no concentrated bile (gallbladder present) is obtained by the use of the usual stimulants.

Positive findings may be accepted with greater certainty than negative findings, as is the case with other laboratory procedures. When there is absence of concentrated bile (gallbladder present) and the result of duodenal drainage is either indeterminate or not in keeping with other features of the individual's problem, recheck examinations should no more be neglected in the appraisal of duodenal drainage than is the case with other examinations.

The value of experience in interpretation has been emphasized by Shay and Riegel[9]. "Persistence and care are required even by the very experienced microscopist. Examination of the sediment after centrifugalization should always be made before the specimen is to be considered negative and it is of great importance that the material be examined shortly after it is obtained."

A. Diagnosis

1. *Suspected Biliary Disease in Absence of Gallbladder*

The value of duodenal drainage in cases of common duct stone after cholecystectomy has been demonstrated in the cases reported by Shay, Tumen, and Rodis[10], and Shay and Riegel[9]. In these instances when roentgenograms of the gallbladder area reveal no opaque calculi, cholesterol crystals and calcium bilirubinate pigment obtained by duodenal drainage may give the clinician the most important objective evidence available. On the other hand, their absence on repeated satisfactory examinations is significant in the diagnosis of biliary dyssynergia.

2. *Presence of Jaundice*

In simple diagnostic problems where there is a history of biliary colic followed by jaundice there is usually no need for duodenal drainage. This is especially true when roentgenograms of the gallbladder area reveal the presence of opaque calculi or when the jaundice has subsided, cholecystography demonstrates the presence of gall stones. But when the history (aside from the presence of jaundice) and roentgen findings are indeterminate, duodenal drainages are helpful in differentiating between so-called "catarrhal jaundice" and a calculous state.

When jaundice is present, regardless of whether or not the patient has a gallbladder, although examinations of the urine and stools for bile pigment are important, the quantity and character of the bile obtained by duodenal drainage may furnish accurate information relative to the cause of obstructive jaundice. Roentgenograms of the gallbladder area may reveal no opaque calculi and cholecystography is not used. Other diagnostic measures which have proved significant in our experience have been quoted by Phillips and Haden[11] and Hartsock[12]. A curve plotted from daily or repeated determinations of the icterus

index is especially significant. Hartsock has mentioned that, "There are many cases in which the exact etiology of the jaundice remains in doubt even after exploratory operation, so it is easy to realize the difficulty of making an exact differential diagnosis clinically."

Early in the course of our appraisal of duodenal drainage this procedure was used as a confirmatory diagnostic measure in the following case:

Case 1: A housewife, 32 years of age, was jaundiced at the time of her admittance to the Clinic. She gave a history of increasingly frequent attacks of pain in the right upper quadrant of the abdomen, chills, and fever, followed by jaundice. The icterus index was 50 units, the blood cholesterol 246 mg. per 100 cc., and a macrocytosis of the red cells was present. Even though roentgenograms of the gallbladder area revealed no evidence of opaque calculi, the diagnosis of gall stones both in the gallbladder and common bile duct seemed obvious. By duodenal drainage a free flow of bile was obtained on each of two separate days and both times the bile contained cholesterol crystals, calcium bilirubinate pigment, many bile-stained pus cells, and tall columnar epithelial cells. On preoperative management, the patient's general condition was considerably improved and the icterus index was reduced to 25 units. At this time cholecystography, using the 2 dose oral method, was reported as showing non-visualization of the gallbladder, and the remainder of the gastro-intestinal series' roentgen examination revealed normal findings.

At operation two stones in the common bile duct at the ampulla of Vater, enormous dilatation of the common bile duct, and a small gallbladder adherent to the surrounding structures were found. No other stones were present. By the introduction of a lead probe through an incision in the common bile duct the surgeon was able to push the stones into the duodenum. The gallbladder was removed and a T-tube was left in place. The pathological diagnosis was chronic cholecystitis. The postoperative convalescence was uneventful and the patient has had excellent health since that time.

3. *Absence of Jaundice*

In cases where jaundice is not present and the cholecystographic findings are normal, biliary disease may still be suspected. The patient may or may not give a history characteristic of biliary colic and other causes for the symptoms have been excluded. In our experience relatively few patients having normal cholecystographic findings have operations on the biliary tract so that the accuracy of cholecystography as a diagnostic procedure in these instances is rarely checked at operation and by the pathologist. We believe the assumption that the biliary tract is normal because the cholecystographic findings are normal in

this group of cases is incorrect. Wilson, Lehman, and Goodwin[13] in dealing with prognosis in gallbladder surgery, state that the ultimate results in 14 cases of normal cholecystographic shadow are only 50 per cent satisfactory. "This is of particular interest not only in the use of the normal cholecystogram as a warning against operation but also to emphasize further the suggestion of Graham and Mackey[14] that a proportion of unsatisfactory results in gallbladder surgery arise from mistaken diagnosis." Jenkinson[15] found that in a series of 95 cases with symptoms referable to the gallbladder, cholecystography showed a normally functioning gallbladder in 70 (73 per cent).

In dealing with operations on the stoneless gallbladder, Graham and Mackey found the percentage of cures or improvement the same in the group of patients with normal cholecystograms and in the group with non-visualized gallbladders (60 per cent). In the same type of case Kunath[16] stated, "of the cases in which there were normal cholecystograms, there were cures or improvement in 75 per cent."

Therefore, in spite of normal findings by cholecystography when a strong suspicion of biliary disease remains, we believe significant abnormality in the biliary tract should not be considered to have been excluded until two or more duodenal drainages result in normal findings. On the other hand, positive findings by duodenal drainage may result in a diagnosis of cholesterosis, a pre-calculous state, or chronic cholangitis. If early surgical procedures do not seem to be indicated, the use of the important developments in medical management should prove especially valuable in these cases.

In the following case the significance of calcifications in the right upper abdominal quadrant was not determined at the time of the initial examination. In view of the important findings obtained by duodenal drainage when it was used at a later date (confirmed at operation), its earlier use might have established the correct diagnosis before the onset of biliary colic and jaundice.

Case 2: A man, 43 years of age, was admitted to the Clinic in March 1935, and a diagnosis of irritable colon, hypometabolism, and obesity was made. Cholecystographic examinations were reported as showing a normally functioning gallbladder not containing calculi, but five calcifications were visualized outside the gallbladder in the right upper quadrant of the abdomen. There was no history of jaundice and the symptoms were interpreted as unrelated to biliary disease. It was thought that the shadows represented calcified lymph nodes. The use of duodenal drainage was not considered at that time.

Two years and three months later the patient was deeply jaundiced at the time of his re-admittance (June 1938). The icterus index was 75

units and it rapidly rose to 100. Eleven days prior to this entrance he had been awakened by severe pain in the right upper quadrant of the abdomen. Hypodermics were given for relief but the pain recurred off and on, and meanwhile he became deeply jaundiced. Roentgen examination revealed no change in the calcifications. On each of four separate days a free flow of bile was obtained by duodenal drainage. This contained cholesterol crystals, large strands of cast-like mucous-material, and an abnormal number of bile-stained pus cells, in addition to pigment granules and bile-stained tall columnar epithelium. A diagnosis of common duct stone was made.

Operation was performed and a stone, the size of a pea, associated with the presence of "gravel," was found in the common bile duct at the ampulla of Vater. The gallbladder was small and presented considerable fibrosis in its walls but it contained no gall stones. The common bile duct was much thicker than normal but was not dilated. It was thoroughly irrigated and a T-tube was left in place. Nothing was done to the gallbladder. The postoperative convalescence was uneventful, the icterus index curve slowly descended to 10 units on the twenty-third postoperative day, and no abnormal symptoms or findings relative to the digestive tract have been observed since that time.

Roentgenograms of the gallbladder area subsequent to operation showed an absence of the calcifications observed at the time of the first examination.

Non-Visualization of the Gallbladder by Cholecystography

Non-visualization of the gallbladder by cholecystography (no opaque calculi visualized) does not mean that the cause for the patient's abdominal symptoms has been found. Unless there is a history of unquestioned biliary colic, it is advisable for the surgeon to defer operation on the biliary tract until roentgen and other examinations of adjacent organs, as well as duodenal drainage, have been done. Close correlation of all clinical and laboratory evidence is, of course, assumed in order to prevent an unsatisfactory postoperative course. In questionable cases, at least recheck cholecystographic examinations should be made after the patient has been on medical management several weeks before it is concluded that abnormality in the gallbladder is the chief cause of the patient's symptoms.

The various causes of non-visualization of the gallbladder by cholecystography are now well known. When the clinical and other laboratory evidence is not conclusive, the findings on duodenal drainage may show that operation is clearly indicated. On the other hand, when satisfactory duodenal drainages result in normal findings in these instances, we believe operation should be deferred until medical man-

agement has relieved symptoms pertaining to other parts of the digestive tract.

Jenkinson[15] found that in 8, or 40 per cent, of twenty patients with non-functioning gallbladders by cholecystography there was a normal response radiographically after medical management.

We agree with Wilkinson[17] in his discussion of "Chronic Cholecystitis Versus Irritable Colon" when he states, "The fundamental difference between the diagnosis of chronic cholecystitis and that of irritable colon would be of little moment but for the fact that one condition is organic and likely to be treated surgically while the other is a functional disorder amenable to dietary management. Since there is such a similarity in the two types of complaints, it does not seem proper immediately to classify chronic dyspepsia as gallbladder disease because of a dull ache in the right upper part of the abdomen and a poorly seen gallbladder. Lahey and Jordan have shown that 44 per cent of the patients with chronic dyspepsia whose gallbladder cannot be visualized will later show normal filling after an adequate period of bowel management. The patients who show delayed emptying or poor visualization will be even more likely to fall into the functional group." This coincides with our experience except that a smaller percentage of our patients having irritable colon have a non-functioning gallbladder by cholecystography at the initial examination with return to normal function later. Differences in cholecystographic technic used at the time the statistics were compiled may be the explanation.

The significant feature is the established fact that spastic conditions of the gastro-intestinal tract can cause temporary non-visualization of the gallbladder by cholecystography. In this group most of our patients did not have duodenal drainages at the time of the original examination because the symptoms relating to the irritable colon syndrome, associated with diarrhea or constipation, or one alternating with the other, seemed most significant. If recheck cholecystography at the end of a period of adequate bowel management does not result in normal findings, we now routinely request duodenal drainage.

In our experience, one of the chief causes of the increasing incidence of irritable colon is the widespread use of magnesium sulfate given by mouth each morning for months if not years as a supposed "cure" of alleged gallbladder disease. We refer to patients who do not give a history of clear-cut biliary colic but have non-visualization of the gallbladder by cholecystography, associated with an indeterminate chronic dyspepsia. Even though the symptoms involve the right upper abdominal quadrant (usually close analysis of symptoms will reveal the presence of abdominal distress related to other parts of the colon also)

we have found that the discontinuance of the increasing use of cathartics, particularly daily saline cathartics, together with other principles of bowel management, result not only in relief of symptoms but a return to normal in gallbladder function.

The difference in giving hypertonic magnesium sulfate *by mouth* and by duodenal tube (after which it is immediately removed by siphonage during duodenal drainage) has been emphasized earlier in this discussion.

Case 3: In the following case, the 21-year-old unmarried daughter of a physician had symptoms characteristic of biliary colic but of equal significance were those pertaining to an irritable colon.

From the standpoint of symptoms and personal observation, this patient repeatedly said that, "as long as I follow the principles of bowel management as instructed I have no trouble. When I encounter circumstances which make this impossible or I want to try myself out I get one of these attacks (pain in the right upper abdominal quadrant radiating to the right scapula without jaundice)." At these times she also invariably had dysfunction of the colon, either unusual constipation or diarrhea, cramp-like pain, and definite tenderness over the lower left colon. A test enema, given in the hospital at the time of an attack characteristic of biliary colic increased the pain as the fluid entered various parts of the colon, but complete relief was obtained after the expulsion of the enema. It should be emphasized that this patient was a shrewd observer and honest.

Repeated double-dose cholecystographic examinations resulted in nonvisualization of the gallbladder without evidence of opaque calculi. Two duodenal drainages resulted in obtaining both cholesterol crystals and calcium bilirubinate pigment and no concentrated "B" fraction of bile. Surgeons who saw her in consultation during the initial attacks advised no surgical procedures, partly because of her age, but also because of misjudgment relative to functional disturbances, in spite of the positive findings by cholecystography and duodenal drainage. Finally, she had an attack of biliary colic which was followed by jaundice. At operation gall stones were found in the gallbladder (two large mulberry stones and ten or twelve small stones the size of a pea). The common duct was dilated, opened, and explored but no stones were found; however, drainage was done. Her convalescence was uneventful and recently it was learned that she is in excellent health and is on a European honeymoon.

A letter from her father, a well-known physician, states, "The pathological section of her gallbladder showed no evidence of infection and it was the opinion of us all that this was purely a problem of metabolism."

It would seem that this case emphasizes the close relationship between the biliary tract and the colon, that spastic conditions in the colon or other parts of the gastro-intestinal tract, may, in a reflex manner, cause spasm of the sphincter of Oddi, which in turn results in metabolic disturbances or the soil (to quote Osler) contributing to the formation of cholesterol (non-opaque) gall stones. Is this any more a stretch of the imagination than to say the disturbance in the biliary tract in a 21-year-old girl resulted in reflex disturbances in the colon? Which is the cart and which is the horse? It is the author's opinion that a careful study of a relatively few intelligent individuals would result in a more accurate solution of these problems than an incomplete study of a large number of statistics.

4. *Suspected Pancreatic Disease*

When suspected pancreatic disease is present the analysis of the findings on duodenal drainage is of unquestioned value. On the diagnostic side, it is important when purulent material or other inflammatory products are obtained, as well as to permit analysis of the character of the duodenal contents, including studies of pancreatic enzymes. Constant duodenal drainage while adequate parenteral therapy is administered has also proved important from the therapeutic standpoint.

5. *Certain Diseases of the Liver*

In the appraisal of certain diseases of the liver, such as biliary cirrhosis, the use of duodenal drainage has proved important in our experience.

6. *Postoperative Appraisal of Biliary Tract*

In the postoperative evaluation of the state of the biliary tract we believe the findings obtained by duodenal drainage have not been sufficiently utilized, in view of the fact that it is desirable to prevent the "post-cholecystectomy syndrome." The writings of Best and Hicken[18] relative to cholangiographic demonstration of biliary dyssynergia are of unusual significance in this respect. Even though meticulous operative procedures have been done, detritus may remain in the common bile duct which is not drained by the T-tube. Substances injected directly into the duodenum, in proper concentration, have proved more effective than the administration of the same substances by mouth, not only in producing relaxation of the sphincter of Oddi, but also in permitting analysis of drainage from the common bile duct.

If duodenal drainage has not been done prior to two months following operative procedures on the biliary tract, we believe the more common use of this procedure at this time, together with appropriate use of medical management, according to the findings, will result in better

operative statistics and the ultimate aim of a satisfied patient. It is fair to assume that the desirable postoperative course in the individual case, particularly when unusual circumstances are present, will be afforded by the mutual interest and cooperation of both the internist primarily interested in gastro-intestinal diseases and of the surgeon.

B. Treatment

Our experience in the treatment of biliary disease by the use of duodenal drainage is limited. Our chief interest in this procedure has been the added information it gives when other diagnostic procedures are either indeterminate or not helpful. We believe it is of value in the treatment of pancreatitis, in shortening the course of "catarrhal jaundice," and in non-calculous biliary tract disease when other well-known methods of medical management prove unsatisfactory. Intractable urticaria; the use of a vaccine made from cultures of bile obtained by duodenal drainage has been mentioned.

Conclusions

1. The increasing use of duodenal drainage in recent years, in correlation with cholecystography, as well as the clinical and other findings, has proved to be an important diagnostic procedure under the circumstances mentioned.

2. The value of cholecystography is well known.

3. The most important indications for duodenal drainage are the instances where the gallbladder has been removed, where jaundice of a sufficient degree to contraindicate the use of cholecystography exists, and when both clinical and cholecystographic findings are inconclusive.

4. In patients having operations subsequent to duodenal drainage, the operative findings confirmed the findings by duodenal drainage in 84 per cent of all cases to date. Duodenal drainage has not been used as a routine procedure in the investigation of the digestive tract. Its use has been limited usually to those instances where other diagnostic criteria are indeterminate.

5. Since routine autopsies in various countries have shown that half of the persons above the age of 30 years had pathological changes in the gallbladder and approximately 20 per cent had gall stones, the more common use of duodenal drainage should result in earlier diagnoses and earlier operations, if medical management is not appropriate, before pathological processes have extended so widely that surgery cannot be expected to relieve the patient's symptoms.

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A DEFINITIVE CURE OF EARLY ESSENTIAL HYPERTENSION

Report of a Case

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The patient, a young man, 22 years of age, was referred to me by Dr. H. Street of Litchfield, Ohio. He consulted me because of emotional instability, sweating, slight tremor, tachycardia, heart consciousness and inability to undertake a normal amount of work. In the course of the examination at the Clinic an early essential hypertension was discovered, the eye grounds exhibiting the changes seen in essential hypertension of Grade I. The blood pressure was 150 systolic, 100 diastolic. Here was a case in which neurocirculatory asthenia was associated with very early essential hypertension at the age of 22. I recognized the opportunity for performing an operation on the branches of the celiac ganglion and the adrenal glands on both sides in so early a phase of essential hypertension that I would not have suggested the operation for the essential hypertension alone, for this was not the disease that was causing the disability for which the patient sought relief. It was the neurocirculatory asthenia which brought him to the Clinic.

This operation was performed seven years ago. Doctor Street and I have followed this patient's progress with very great interest as we realized that in this case we had a rare opportunity to throw light upon an important question, namely: Is essential hypertension a pure pathological process like the growth of a fibroid tumor or may essential hypertension be the result of a pathologic physiology? In other words, is essential hypertension a curable disease in its early stage?

On May 1, 1939, Doctor Street was kind enough to send the patient to me for a check-up. Since the operation he has married, has two children, works every day, has charge of two gasoline stations. The flushing of the face, the sweating, the tremor and the tachycardia associated with the neurocirculatory asthenia seven years ago have completely disappeared. He is now emotionally stable. His hands are dry, the abnormal sweating and the tremor have disappeared.

Of particular and significant interest are the facts that his blood pressure is now 120 systolic, 70 diastolic, and that Doctor Ruedemann found the eye grounds normal. The changes in the fundus, characteristic of essential hypertension of Grade I, have disappeared. The patient, himself, reports that he has been able to work steadily, and that he has none of the old symptoms, but feels entirely normal.

This case supplies evidence of the neurogenic origin of essential hyper-

tension, that is, that the disease is not a pathology of structure but is a pathology of function.

Comment

I have three other cases similar to that of this patient, which we are following, in which denervation of the adrenal gland and celiac ganglionectomy were performed in the very early phase of hypertension, approximately the same phase as in the case of this patient.

These and other cases suggest an analogy with the late and early operation for cancer of the breast. It is well established that when cancer of the breast is operated upon as early relatively to advanced cancer as the essential hypertension in this case was relative to advanced hypertension a permanent cure is effected in practically every case. I refer to the case of early cancer of the breast in which no involvement of any tissue but breast tissue and no involvement of axillary glands are found. In this case of essential hypertension, which is an incurable disease in a late stage, a cure was established by an operation performed before the disease had reached an irreversible stage.

In our early experience with cancer of the breast, permission for operation often was not granted because surgeons had cured or benefited so few patients, largely because they were not given the opportunity to perform operations earlier and to a degree because surgeons themselves had not acquired a sound principle for operation. From our experience in 534 operations on 313 patients with essential hypertension, we find that we are in about the same position, for patients too often do not appeal for help until the essential hypertension has gone on to the malignant phase in which there is sclerosis of all the blood vessels of the body, headache, weakness, incapacity to work, pounding of the heart and the patient is awaiting the final heart attack or apoplexy or uremia to take him out of his misery. This corresponds to the advanced stage of cancer of the breast. Many years ago the surgeon saw almost as many cases of cancer of the breast in which there were fixation to the chest wall, frozen axilla, and in many cases ulceration, as he now sees of hypertension in the malignant phase.

If cancer of the breast is operated upon in the early stages it is curable. This case indicates that if essential hypertension is operated upon in its early stage it is equally curable.

The mortality rate of celiac ganglionectomy is now well controlled. In our last 74 operations there has been no death.

ENCYSTED SUBDURAL HEMATOMA

W. James Gardner, M.D.

Although hematomas of the "dura mater" were described by Virchow in 1857, the relative frequency of this lesion has been fully realized only during the past ten years. The lesion consists of an encysted collection of old blood attached to the inner surface of the dura over the convexity of one or both cerebral hemispheres. In this communication, I shall consider only the encysted form of hematoma and shall not include traumatic subdural effusion (fluid hematoma of Munro[1]) or the acute subdural hematoma which produces immediate symptoms and is generally accompanied by a laceration of the brain. The latter two lesions are so different in their morphological and clinical aspects as to deserve separate consideration.

The accident responsible for the encysted subdural hematoma is a minor one, as a rule, and the force of the blow usually is exerted in an anteroposterior direction. The resulting dislocation of the brain within the cranial cavity stretches and tears one or more of the short cerebral veins communicating with the immobile sagittal sinus. There occurs at once a large extravasation of blood over the convexity of the hemisphere in the subdural space. The bleeding ceases when the intracranial pressure reaches a level at which no more blood can leave the torn vein. This degree of intracranial pressure is not incompatible with life and the immediate symptoms may be mild and transient.

The subsequent behavior of the subdural clot is unique. The usual regressive changes and absorption do not occur with a clot in this location. Within a few days or a week the clot is surrounded by a mesothelial-like membrane after which the contents liquefy, forming a hemorrhagic cyst. During this stage symptoms may be absent or trivial. The contents of the cyst, however, undergo a slow progressive augmentation[2] due to the accession of cerebrospinal fluid which is drawn through the semipermeable lining by the osmotic tension of the contained blood proteins. Accompanying this increase in size of the cyst, symptoms of increasing intracranial pressure supervene and most of these patients probably die without the true nature of the condition having been recognized (Fig. 1).

A summation of our experiences with these lesions produces the following composite picture: A man, aged 50 years, slips on the ice and falls, striking the occiput. He gets to his feet, slightly dazed for a minute, following which he has pain in the head for a few hours, but this is not severe enough to warrant his going to bed. Thereafter he feels quite well and dismisses the accident from his mind. Three weeks later he begins to have headache which increases in severity. The relatives then notice changes in his behavior, accompanied by mental

confusion and increasing somnolence. These signs and symptoms show gradual progression, and finally the patient is in a stuporous condition when admitted to the hospital three months after the accident. On examination he is aroused with difficulty. The neurological signs are vague and conflicting. There is no choking of the optic discs, and the

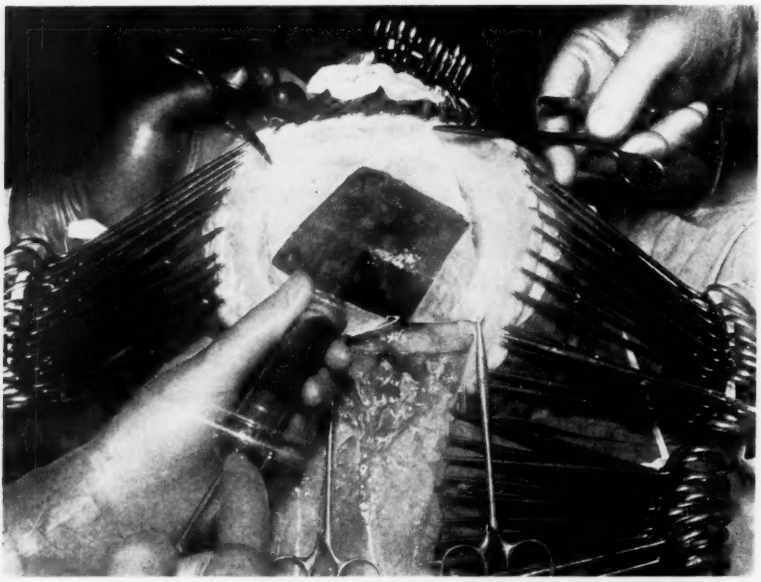

FIGURE 1: An encysted subdural hematoma exposed at operation. The dura has been reflected from its outer wall and coffee-colored fluid is being aspirated.

spinal fluid pressure is only slightly increased. The fluid is somewhat yellow. Roentgenograms of the skull yield entirely normal findings. While under observation, there may be marked fluctuation in the state of consciousness and the neurological signs may appear and disappear. When confronted with this clinical picture, the most rational procedure is to make a trephine opening in each parietal region in the expectation of finding and draining a subdural hematoma.

Practically every author who has written upon this subject has stressed the fact that the trauma which is responsible for the formation of the chronic encysted subdural hematoma is generally mild. This is attested by the fact that there was x-ray evidence of a fracture of the skull in only one of 37 cases observed in recent years at the Cleveland Clinic. In this case the fracture was on the side opposite the hematoma. Furthermore, of these 37 cases only six patients were rendered actually unconscious by the injury. One patient was amnesic for a few

days after the injury, although not actually unconscious; several were dazed for a few minutes by the force of the blow. In the remaining cases there was no alteration at all in the state of consciousness produced by the blow. In only four of the 37 cases, a history of the responsible trauma could not be obtained. Of these, one patient had been subject to frequent attacks of epilepsy for 25 years. Another was a boy of 11 years who was quite ataxic due to the presence of a cerebellar tumor. The third patient had been in an automobile accident but stated that he had not injured his head. With this information it seems very likely that the hematoma was the result of an unappreciated or forgotten head injury in each of these three cases. The fourth case in which no history of trauma could be obtained was that of a colored preacher of 62 years with definite slowing of his mental processes due to arteriosclerosis. Because of the memory deficit I do not believe that we can accept his word that head trauma had not occurred.

My experience, therefore, indicates that these lesions are invariably produced by trauma and the burden of proof is upon him who would assume otherwise.

"Spontaneous" Subdural Hematoma

Since the days of Virchow various authors have tried to differentiate between the "traumatic" and the "spontaneous" or "reactive" types of subdural hematoma. While a spontaneous type may exist, I doubt very much that it ever assumes the typical encysted form of the traumatic variety. The "spontaneous" form is supposed to occur more frequently in the insane, in the decrepit, and in states of acute and chronic alcoholism. For those who maintain that spontaneous hematomas form in these conditions I would like to ask this question. Are there any states other than these in which head trauma is more likely to occur and in which it is less likely to be proven? The answer is no! Many traumatic hematomas have been described as spontaneous simply due to the failure of the examiner to obtain an adequate history.

For instance, Kaump and Love[3] describe the postmortem findings in 30 cases of subdural hematomas. They state that 13 of these hematomas were of the traumatic type and 17 were spontaneous. Such a high incidence of the spontaneous lesion is at variance with all published statistics. The difficulty of obtaining the history of trauma has been stressed by many careful observers. Repeated questioning of the relatives is frequently necessary in order to establish the fact that the patient has injured his head. In some instances the history can be obtained only after the patient's memory has returned as a result of drainage of the hematoma. Naturally, therefore, when the lesion is identified only at necropsy, the difficulty of obtaining the history of trauma is intensified. Furthermore, in 14 of the 17 cases of so-called spontaneous

hematomas reported by Kaump and Love, the sex and age incidence and the gross and microscopic appearance of the lesions differed in no way from those in which a definite history of trauma could be established. Their three spontaneous cases in which there were associated blood dyscrasias did present some gross and microscopic differences and I am prepared to admit that these hematomas were probably genuinely spontaneous.

Recently a theory has been advanced that the subdural hematoma is really an intradural hematoma; that the hemorrhage occurs into the middle, vascular layer of the dura so that the membrane constituting the inner wall of the hematoma is really the inner layer of the dura [3, 4]. In my opinion this theory is far from established by the work of these investigators. The difficulty of proving by histological study whether a hematoma is subdural or between the layers of the dura when the lesion is one to four months old is very obvious.

Analysis of Cases

In this series of 37 cases, 33 of the patients were males and four females. The lesion occurred most commonly in the sixth decade of life as shown by the accompanying chart (Fig. 2). In analyzing the nature of the accidents in these 37 cases, we find that automobiles figured in only 10 cases. This is a very low incidence when one considers present day craniocerebral injuries as a whole. In ten cases the patient struck his head in falling from a standing position to the floor or ground. Six of these falls were due to icy pavements. In five instances the patient had merely struck his head against a door or low-hanging beam.

In one of the cases the hematoma occurred following a right subtemporal decompression for a condition which has been called "cerebral pseudotumor." This patient was a man of sixty-seven whose only complaint was failing vision which was found to be due to choking of the optic discs. At encephalography, 152 cc. of cerebrospinal fluid were recovered. The resulting films showed the ventricles to be normal with a very marked dilatation of the cerebral sulci on both sides of the brain. There was not the slightest evidence of an expanding intracranial lesion. Immediately after encephalography, a right subtemporal decompression was performed and there was no evidence of a subdural hematoma at that time. The patient's convalescence was uneventful, the intracranial pressure was controlled for a time, and then it recurred. Nine weeks after the encephalogram and decompression, a bilateral parietal trephine was carried out in order to permit the supposedly excessive amount of cerebrospinal fluid to drain into the layers of the scalp. On the right side, much to our surprise, a typical subdural hematoma was encoun-

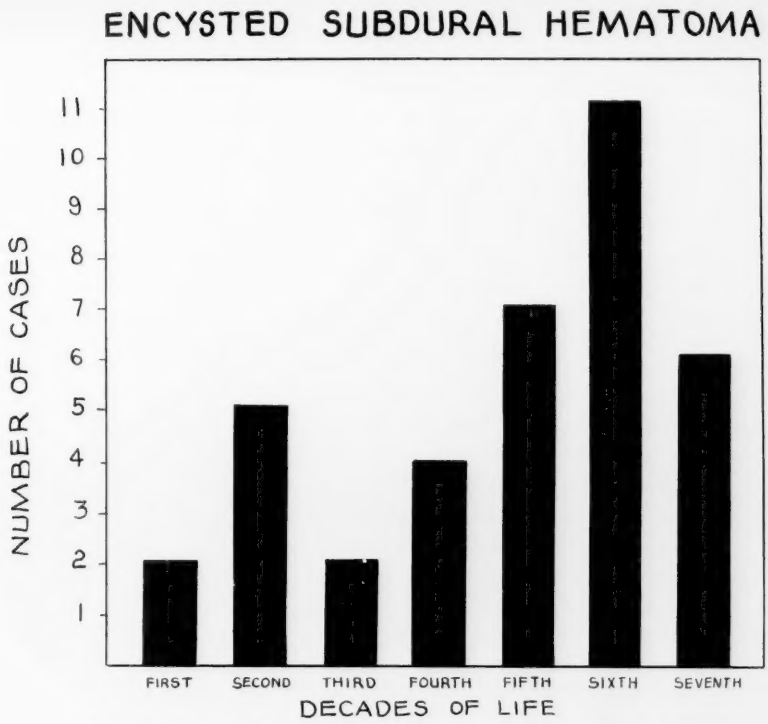

FIGURE 2: Age incidence in 37 cases of encysted subdural hematoma.

tered, and a large quantity of old, dark, fluid blood was removed. We believe that the bleeding in this case occurred as the patient struggled in coming out of his anesthesia, that the hemorrhage was favored by the fact that his blood vessels were brittle with age, and the mobility of the brain within the cranial cavity was increased because the cerebrospinal fluid was replaced with air.

In analyzing these 37 cases as to the site of the trauma, we find that the injury was exerted in an anteroposterior direction in 22, on the side of the head in five, in three cases on the vertex, while in seven instances the exact location of the head injury could not be ascertained. The latent interval between the time of the injury and the onset of definite cerebral signs averages about three weeks, while the lapse of time from the accident to operation is approximately twelve weeks. Where the lapse of time is very much longer than this, there is increasing doubt as to whether the implicated trauma was really the responsible one.

Spinal puncture was performed in 31 of these 37 cases. The pressure of the spinal fluid was definitely increased in 16 instances, while in 19

cases the fluid was xanthochromic. There were no characteristic changes in the cell count of the spinal fluid nor in its total protein content.

Headache was the most common symptom. It occurred in 28 of the 37 cases. Changes in the intellectual sphere were quite marked in 25 cases. They usually consisted of somnolence, stupor, or mental confusion. Vomiting occurred in ten instances and disturbance of vision in seven. The neurological signs indicated the location of the lesion correctly in 17 instances. In six cases the neurological signs implicated the wrong side. In five cases in which the lesions were unilateral, the neurological signs implicated both cerebral hemispheres. This occurrence of homolateral cerebral signs in these cases is occasioned by the tremendous dislocation of the brain which may cause pressure of the opposite cerebral peduncle on the sharp free edge of the tentorium. In nine instances there were no localizing signs. The hematoma was on the right side in 20 instances, on the left side in 13, and in four cases there were bilateral hematomas.

Of these 37 cases, the lesion was found at operation in 35 instances, and in two patients it was discovered only at autopsy. Of the 35 patients who were operated upon, 33 recovered, and two died. Twenty of the patients operated upon were treated by a formal craniotomy and all recovered. In one patient with bilateral lesions, craniotomy was performed on one side and a trephine on the other. In 14 cases the operation consisted merely of trephine, irrigation, and drainage. Two of these 14 patients died. One was moribund at the time of the operation, while the other patient died from a hemorrhage into the pons which occurred apparently at the time of operation. In no case was there recurrence of intracranial bleeding after operation.

It is important to suspect a subdural hematoma when the clinical picture suggests a high degree of intracranial pressure and the spinal puncture fails to reveal it. Observance of this dictum has permitted us to rescue several patients who otherwise would most surely have died.

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PERIPHERAL TUMORS OF THE JAWS

CHARLES A. RESCH, D.D.S.

The word tumor has been defined as any swelling or morbid enlargement. A tumor is a phase of an inflammatory process and it is used to describe neoplasms or blastomata. These tissue masses occurring within the buccal cavity should be of particular interest to members of the dental profession because they are often the first to be consulted by the patient. This paper will be limited to the discussion of tumors located on the peripheral tissues and commonly known as epuli. The large group of centrally located tumors which, in the course of time may involve the peripheral tissues, will not be considered.

The common tumors of the peripheral tissues of the buccal cavity are inflammatory in origin. Infections such as actinomycosis, tuberculosis, and syphilis which are known as the granulomatous diseases may be characterized by tumor or swelling of the peripheral tissues of the mouth. The possibility of their presence should be considered in the differential diagnosis of all oral lesions.

Undoubtedly, the most common peripheral tumor of the jaws is the simple hypertrophy or tumor-like overgrowth which is known as the epulis granulomatosa or granuloma pyogenicum. These simple tumors exhibit characteristics of both true inflammation and true blastoma. They may occur anywhere in the mouth but they are found most frequently on the marginal gingiva. They vary in size and may have normal epithelial covering. They may occur in the socket of a recently extracted tooth where a foreign body, a tooth fragment, or usually a small bony sequestrum is found to be the underlying cause. It is generally believed that mechanical irritation is an important pathogenic factor, such as from carious teeth, poor fillings that overhang, poorly adapted dentures, and excessive calculi. For this reason they are most often found in those mouths where oral neglect is much in evidence. These epuli appear to be closely related to the fibromata and they may recur after incomplete removal.

Examination microscopically reveals hyperplasia of connective tissue with evidence of chronic inflammation and hypertrophy of the overlying epithelium. The so-called gum boil which is the peripheral terminus of the sinus tract from a periapical abscess belongs in this group as do also the so-called pregnancy tumors of the gingiva which are associated with altered endocrine function. An extenuation of this condition, usually occurring in adolescence and characterized by generalized hypertrophy of the gingiva, has been described by Prinz and Greenbaum[1] under the tile of "Diffuse Fibromatosis of the Gingiva." The etiology of this condition is unknown. It is characterized, in addition to the

marked gingival hypertrophy, by a loosening and displacement of the teeth, with gradual resorption of the underlying alveolar bone.

Benign giant-cell tumors which may occur peripherally as well as centrally are believed by Geschickter and Copeland[2] to constitute an earlier stage of the peripheral fibroma. This tumor, as the name implies, is characterized histologically by foreign body giant-cells, with centrally located nuclei in a fibrous stroma. It has been pointed out that in the mouth they have a predilection for parts of precartilagenous origin or anterior to the molar teeth at the site of those deciduous teeth which are shed through osteoclastic reaction on their roots. Their etiology is uncertain, but some irritating factor is usually present. Ewing[3] and Bloodgood[4] believe the tumor is a true blastoma while others support the inflammatory or reparative theory as advanced by Geschickter and Copeland. The clinical picture is that of a dark red to purplish swelling, firmly attached to the bone. Moderately indurated, it is not fluctuant, and it may, over a period of time, erode the alveolar bone so as to produce roentgenographically an area of bone destruction through which may be observed coarse trabeculations. A walling-off zone of condensing osteitis may be observed attempting to limit the progress of the erosion.

The benign peripheral fibroma belongs in the group of true blastomata. These tumors are well defined and slow growing, occurring anywhere on the investing tissues of the mouth. They are characterized clinically by nodular masses of tissue covered with normal epithelium. They may be hard, soft, or of a mixed type. The histological picture is that of pink staining bundles of collagen fibers, loosely arranged in the soft type to dense interlacing bundles of the hard type with slight vascularity. Round-cell infiltration, characterizing inflammatory reaction, is never pronounced but may frequently be observed in some part of the section.

The malignant fibroblastoma or fibrosarcoma may occur on the investing tissues of the buccal mucosa. Early growth may be slow with a rapid change as a later manifestation. Clinically, it appears as a deep red to bluish-red mass of hard, elastic character, developing on a broad base. It is quite vascular and bleeds freely on injury. The alveolar process of either the maxilla or mandible, often in the region of the ramus, is the most frequent site. Histologically, it is a very cellular tumor with spindle-type cells, fairly uniform in size, with a dense cytoplasm and deep staining nuclei showing frequent mitotic figures. The fibrous stroma identifies this type from the osteogenic type which, while originating centrally, may involve the peripheral tissues. Thoma[5] has stated that it does not appear to be as common today as compared with two or three decades ago and he believes this is probably due to more

careful differentiation and diagnosis, giant-cell tumors having been classified as sarcomas in the past.

There are a few other true tumors or blastomata which occasionally, although exceedingly rarely, occur on the peripheral surface of the jaws. One of these is the myxoma of mesenchymal origin, with cells developed to produce mucin, lipoma composed of fat cells and with a gross appearance of a yellow elastic mass, and the neuroma, with nerve cells. The true neuroma is one of the rarest of tumors that can occur in this region and must contain actual nerve cells or neurocytes. The term is often used in association with amputation neuroma which is not in the true sense a neuroma as it is a product of inflammatory fibrous tissue of the neurolemma, or sheath, which contains no nerve cells.

The endothelioma is another rare blastoma of the peripheral tissues, usually occurring on the palate at the junction of the hard and soft palate to the lateral aspect. It forms a spherical, circumscribed mass, with normal epithelial covering. The cells of this tumor are derived from the mesenchyma and are closely related to connective tissue which gives a varied histological appearance, making microscopic diagnosis most difficult.

The angioblastoma may be made up of blood vessels as in the hemangioma or lymph vessels as in the lymphangioma. The hemangioma, of which there are several recognized types, occurs in the region of the embryonic fissures on the skin, lips, nose, and mucous membranes of the mouth. In the mouth it may be said to occur most frequently on the papillae between the teeth. These tumors have a soft, spongy, vascular, rounded appearance, ranging in color from red to deepest purple, depending upon size and type of blood. The lymphangioma is usually found on the lip or tongue, occurring as a congenital formation.

The lymphoblastoma, or tumor whose cells belong to the lymphocytic series, are slow growing and often are mistaken for chronic inflammatory processes. This tumor is known under a variety of names such as the lymphocytoma, lymphoma, lymphosarcoma, small cell sarcoma, lymphatic leukemia, or Hodgkin's disease. The wide variation of names is due to the varied clinical pictures, according to location, rapidity of growth, and manner of spreading. Thoma[5] records a case of a lymphosarcoma of the gingival tissue in a patient, a man 66 years of age, who complained of swollen gums. On examination the gingival tissue which was generally inflamed revealed a small tumor mass under a bridge on the lower right side. The impression was hypertrophy due to mechanical irritation. Biopsy revealed a lymphosarcoma. New tissue rapidly developed on the gingival tissue with swelling of the submaxillary and submental glands. In spite of roentgen treatment, the patient's condition rapidly became worse with expiration four weeks after biopsy. Several

cases of leukemia treated at the Clinic have shown extensive hypertrophy on the gingival tissues and, while not confirmed by biopsy, appeared undoubtedly of lymphoblastic etiology. Gross oral neglect appears to be a definite predisposing factor.

The melanoblastoma is a tumor of mesenchymal origin and is extremely rare in the oral cavity. It is usually flat, covering a wide base and it is conspicuous chiefly because of its color which ranges from dark brown to black. It grows rapidly with metastasis early, treatment being of little avail. The tumor is found chiefly on the hard palate and, according to Thoma, the gingiva of the maxillary alveolar process. This lesion should not be confused with so-called blue gum which is frequently found on the alveolar tissue in members of the colored race.

Mixed tumors of the palate have been reported[6]. In these, tumor development occurs in at least two germinal derivatives, producing a combination of two neoplastic developments in one tumor. Teratoma, or tumors of tissue and organs of one, two or three germinal layers, may be found in the oral cavity on the palate, jaws, floor of the mouth, and tongue.

The papilloma is the benign, epithelial tumor which is frequently found on the soft tissues of the oral mucosa. These appear as pedunculated masses of soft, pale, cauliflower-like growths occurring on the cheeks or tongue as a rule. At microscopic examination, the marked keratinization which is readily seen is somewhat characteristic of this type of tumor. Epithelial proliferation marked by irregular epithelial downgrowths into the papillae of the corium or true skin is characteristic. This lesion is considered as a possible forerunner of its malignant relative the carcinoma.

Carcinoma of the oral structures in comparison with other oral abnormalities appears as an all too frequent occurrence.[7] The annual mortality rate from cancer in the United States has been given as approximately 90,000 of which some 3,000 growths were within the oral cavity. If there is to be any control whatever, predisposing factors must be eliminated. It does not seem to be mere coincidence that most carcinomas of the oral structures occur in those mouths where, due to oral neglect, oral sepsis is permitted to run rampant. This is a recognized predisposing factor which has been emphasized repeatedly. Other precancerous lesions of particular significance are in addition to the papilloma persistent cracks and fissures, smokers' burns, senile keratosis, and leukoplakia. Leukoplakia with cracks and fissures are to be regarded as the incipient stage of malignancy. Induration and fixation of the base with evidence of rapid change in any of these longstanding precancerous lesions have been pointed out so often that they are now considered axiomatic clinical evidence of malignancy.

It is not the purpose of this paper to discuss the details of the many pathological aspects of this disease. In the clinical manifestations, pain seems to be an early symptom. A fixed area of induration on palpation is always found. Ulcerations, if present, have a dirty grayish base with piled-up indurated edges. The adjacent lymph glands are involved early with ultimate perforation and ulceration of the skin. Metastasis to organs below the clavicle is relatively infrequent. The roentgen ray is of positive value in ascertaining involvement of adjacent bones but of little value apparently in treatment. The erosion of the peripheral bone is usually visible in the early stages; it can also be misleading, however, as Thoma has pointed out, and great care must be taken in forming conclusions as to the amount of bone involved as shown by the radiogram. The marrow spaces of the spongiosa of the bone may be infiltrated by the growth without changing the radiobility to any great extent. The ultimate outlook after the diagnosis has been confirmed by histolopathological study is grave. The use of radium or radon seeds in close proximity to bone produces a slowly healing osteomyelitis of the clinical sclerosing type accompanied by intense pain as has been pointed out. Hemorrhages must be expected as the vessels of the buccal mucosa are eroded. As the resistance of the patient decreases from anorexia, loss of blood, and mounting cachexia, secondary infection with osteomyelitis is a complicating factor. Termination of the disease occurs within one to one and one-half years with rising cachexia, suffocation, and pneumonia as common causes of death.

The following cases represent a few of the oral tumors most frequently observed by the Dental Department during the last year.

Case 1: A 66-year-old white woman complained that a growth in the mouth had been present for one month. She stated that she had noticed a small area on the left side of the upper gingiva toward the cheek which bled when she brushed her teeth. No pain had been experienced. One month previous to our examination she first noticed a small lump with redness and a little soreness but no pain in this area.

Oral examination revealed a mass in the upper left second molar area on the crest of the ridge into the buccal aspect about 2 cm. in diameter. It was spherical in shape on a broad base and had a reddish color with a sharp line of demarcation from the surrounding oral mucosa. It appeared somewhat indurated and movable, the overlying membrane was thinner than normal mucous membrane, and the mass was clear to transillumination. A roentgenogram revealed slight erosion of the alveolar bone.

Impression: (1) fibroma, (2) possible peripheral giant-cell tumor.

The mass was removed under local anesthesia, using the loop cautery followed by electrocoagulation to the base.

The pathological report was: "Section of tissue from the jaws shows a superficial ulceration with complete loss of mucosa in a wide zone of granulation tissue which formed the base of the ulcer. There is a thick layer of edematous connective tissue which is diffusely infiltrated by inflammatory cells of various types. There is no evidence of neoplasm of any kind. Sections of numerous small fragments of curettings from the jaw show cancellous bone with fibrous marrow, large areas of dense fibrous tissue, with chronic inflammatory reaction but no evidence of tumor."

Diagnosis: Chronic inflammatory tissue of the jaw (epulis granulomatosa).

Case 2: A woman, 44 years of age, complained of a swelling in the upper jaw. This swelling had been present in the upper left cuspid region of the maxilla for seven or eight weeks. Pain was first noticed about six months previously. The patient consulted her dentist who at that time found only slight swelling. Four months later the present lesion was observed. It had increased slightly in size but had not been associated with pain. About two weeks previous to the time the patient came to the Clinic the area was opened and bone spiculae were removed but no apparent improvement resulted.

Oral examination revealed a deep purplish-red, palpable, slightly suppurative swelling with some induration. Located in the upper left cuspid region, the mass was approximately 2.5 cm. in diameter. A radiogram the patient brought with her revealed markedly eroded bone with gross trabeculations, but these were not visible on the radiograms taken at our examination. There was a marked condensing osteitis at the inner margin of the eroded bone.

Under avertin anesthesia, the mass was removed by scalpel and the base thoroughly treated by electrocoagulation. Healing was uneventful, without pain or bleeding. Subsequent report six months later revealed normal healing and no recurrence. The patient is now wearing an upper denture with comfort.

Pathological report: "Section shows mucosal epithelium on one surface with a small area of ulceration. In the deeper tissues there is a very cellular, highly vascularized stroma with many multi-nucleated giant-cells present. There are also areas of young cancellous bone."

Diagnosis: Benign giant-cell epulis.

Case 3: A woman, 28 years of age, had marked oral neglect and a mass of soft tissue in the lower jaw between the left cuspid and lateral incisor. This patient was an extremely hysterical woman who had had palsy of the right side of the face since the age of eleven years and she had had frequent attacks of globus hystericus. Because multiple ex-

tractions were necessary, she had been referred to the Clinic. The patient stated that this mass of tissue had been present for approximately 6 to 7 months, apparently growing slowly.

At examination the mass appeared as a hard, immovable, localized hypertrophy of the gingiva between the lower left cuspid and lateral incisor, forcing these teeth apart. A radiogram of the area showed no abnormality. This mass appeared to be attached by a broad base to the buccal aspect of the soft tissue.

Under avertin anesthesia the mass was removed with scalpel, followed by electrocoagulation to the base of the area. The lower impacted third molar on the right side was removed at the same time.

Pathological report: "Section of gingival mucosa partially covered by stratified squamous epithelium with an area of ulceration and complete loss of epithelium and marked inflammatory reaction and considerable fibrosis of the submucosal tissues."

Diagnosis: Chronic inflammatory tissue of the jaw.

Note: Comparison of the histopathological picture of this tissue with that of the first case impresses one with the increased amount of fibrosis present in this tissue. Thus it appears to be a possible transitional stage from chronic inflammatory tissue epulis to a true fibroma.

Case 4: A school girl, 12 years and 10 months old, complained of marked overgrowth of the gingival tissues. This patient was in the seventh grade of school and was making excellent grades. The condition of her mouth had been normal until the age of six years when, on loss of the deciduous teeth, a gradual overgrowth of the gums began. The greatest growth had been noted during the preceding year. No pain had been associated with this generalized hypertrophy.

Examination revealed a generalized marked overgrowth of the gingival tissues, in some instances completely covering the permanent teeth which were loose and malposed. The tissue was characterized by deep pockets or crypts lying along the adjacent teeth. The crypts appeared very tender and smears taken for culture of Vincent's organisms were strongly positive.

The physical examination was essentially negative. Roentgen findings, however, revealed the epiphyseal bone age to be 14 to 15 years and there was marked absorption of the alveolar bones of the jaws. The patient had previously consulted an oral surgeon whose report of a biopsy was: "The pathological process is a hypertrophy of the connective tissue associated with marked edema. It cannot be considered the result of some local infection, the pathological picture is not at all that of a lymphoblastoma." Following the advice of their family physician, the parents did not wish any surgery performed at this time. Accord-

ingly, local treatment to the gingival tissue, using well-known medicaments for the treatment of Vincent's infection and roentgen therapy to the mouth in doses of approximately 1000 R units over a period of four months resulted in no apparent improvement in the condition.

Diagnosis: Diffuse fibromatosis of the gingiva (Prinz and Greenbaum).

Case 5: A business man, aged 75 years, complained of an ulcerating lesion of the soft tissue located in the midline of the maxilla. The patient had first noticed a canker sore on the upper gum with a swelling of the lip twenty-three days previous to our examination. At this time he went to a dentist who checked the teeth and found them essentially negative so he referred the patient to a physician. The physician first took a biopsy which was not reported and treated the patient for trench mouth until a second biopsy was reported as round cell carcinoma. Roentgen treatments were then administered. This was 6 days prior to the patient's entry to the Clinic.

Examination revealed a lesion in the upper maxilla at the midline at the junction of the lip and gum and involving both. This ulcerated lesion was about the size of a nickel with a rather dirty base with indurated edges. The oral condition appeared rather poor with some evidence of oral neglect. Radiograms of the teeth revealed some devitalized teeth showing periapical involvement. The patient had been wearing a dental appliance in the upper anterior part of the mouth. The patient does not smoke.

Under avertin anesthesia, the area was thoroughly cauterized, using electrocoagulation after biopsy.

Pathological report: "Section shows an infiltrating squamous cell carcinoma composed of small nests of epithelial cells with very little tendency to form kerato-hyaline material or pearls. There is a great deal of rather dense stroma in which there is a diffuse inflammatory reaction."

Diagnosis: Squamous cell carcinoma.

Two years later, there was a recurrence with metastasis to the right submaxillary gland. Subsequent roentgen treatment to this area resulted in marked tissue reaction with extensive hemorrhage. On recovery, further electrocoagulation to the area in the mouth was performed. This has been followed by an apparent osteomyelitis with subsequent swelling in the left submaxillary area and formation of an abscess.

Case 6: A man, 66 years of age, complained of a lesion of the mouth. He gave the following history. About five weeks previously he noticed a roughening of the mucosa on the left lower jaw. He had been wearing a lower denture for a period of time but the denture needed adjustments

so he had made these by smoothing the area with sandpaper. The lesion had not increased in size since it was first noted.

Examination revealed a mouth completely edentulous with a raised nodular growth extending along the mandible for about three to four centimeters in the bicuspid region in the floor of the mouth. There was evidence of indurated, infiltrating tissues with an ulcerated crest. A biopsy from this area was reported as follows: "Section of mucosal tissue from the jaw showed an infiltrating, fairly well differentiated, pearl-forming, squamous cell carcinomatous type of growth."

Diagnosis: Squamous cell carcinoma of the jaw.

A total of 3900 roentgen units were given over a period of 18 days. Under this treatment there appeared to be some improvement in the lesion. Six months later, however, the patient again began to have pain and there was noticed a firm mass on the lingual mucosa which was flat and fairly movable with no ulceration. Three months later radon seeds were implanted in the floor of the mouth. Two months later further radon seeds were implanted in the floor of the mouth in the indurated areas. The patient was having considerable pain. He was unable to sleep at night, and considerable necrotic foul tissue was present. One year later the area below the left mandible broke down with a discharge of pus. There was, however, some relief in the pain with marked difficulty in swallowing. There has been a gradual loss in weight.

Case 7: A farmer, 60 years of age, complained chiefly of a sore in the cheek. This patient had been wearing an upper denture for 20 years and a lower denture for 5 years. In the preceding several months he had noticed some temporary intermittent soreness of the left cheek opposite the molar teeth of the denture, but this had not lasted more than 24 hours at a time. Three months previously he noticed a painful sore at this site which made it impossible for him to wear the denture or masticate food. A small kernel in the left submaxillary region had been present for five years but this had enlarged in the past three months and become painful and tender. This patient had chewed tobacco for many years.

Examination revealed in the left side of the mouth opposite the molar teeth an indurated, roughened lesion about the size of a dollar. It was quite tender and arose from the alveolar process in this area. There was a nodule the size of a hazelnut in the left submaxillary region which was tender and fixed.

Diagnosis: Carcinoma of the mouth with glandular metastasis.

Treatment: Under avertin anesthesia the area was treated by electrocoagulation. The postoperative sequence included several secondary hemorrhages but two months later the area appeared well healed with

no evidence of neoplasm. However, four months after operation, examination revealed recurrence. Operation was again performed, using electrocoagulation with implantation of radon seeds to the skin below the mandible. A pathological fracture occurred at this time due to the extension of the growth in the osseous structure. No pathological report was made and the diagnosis has been based principally on clinical examination.

Summary

The importance of oral health as a vital part of general health is to be emphasized. Innocent oral lesions should not be regarded lightly; they warrant early and complete removal with elimination of etiological factors. Too much stress should not be placed on the condition known as Vincent's infection with disregard for a careful search for underlying factors.

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OBSTRUCTIVE LESIONS AND INFECTION IN THE URINARY TRACT

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The common urological dictum that obstructive lesions and infection of the urinary tract are bad bedfellows has been established by universal clinical experience. Not only does obstruction predispose to infection, but treatment of the infection in the presence of obstruction is usually quite hopeless until the obstruction is relieved. Thus the recognition of obstruction is essential to proper treatment of urinary infections and in the present era of effective chemotherapy, one criterion which may be used in suspecting the presence of an obstructive lesion is the failure of the infection to respond to chemotherapeutic agents. Chronic urinary infection should, therefore, be considered to be due to urinary stasis until proved otherwise. The relief of the obstruction is a surgical problem in the majority of instances.

Obstructive lesions in the urinary tract are of many types and may be partial, complete, or intermittent. They may occur anywhere from the calices to the urethral meatus and may be either congenital or acquired. An important consideration from the point of view of management is the location of the obstruction, that is, whether it is below or above the bladder and, in turn, whether the supravesical lesion is unilateral or bilateral.

That obstruction predisposes to infection finds many examples and sooner or later infection is almost sure to complicate any obstructive lesion. The increased susceptibility of an obstructed urinary tract to infection is due to the resulting congestion in the kidney which reduces the resistance of the renal cells and pelvic epithelium to bacteria which may be excreted and this, added to stasis of urine to provide a good culture medium, sets the stage for infection. It has generally been accepted that the kidneys may excrete bacteria as, for example, during the course of any acute infectious disease and in the absence of any obstruction, no symptoms referable to the urinary tract may occur whereas if obstruction is present infection is likely to follow. Once infection is present, however, obstruction plus infection is rapidly destructive to renal tissue. In fact, extensive destruction of the renal parenchyma rarely results from infection alone without some degree of obstruction and, in general, the more complete the obstruction, the more rapid the renal damage.

True it is that many obstructive lesions may be present for a considerable period of time without giving rise to any noteworthy symptoms and many of these cases are first brought to the attention of the physician by the advent of infection. This may occur in young children, especially those with a congenital type of obstruction, although in some cases a

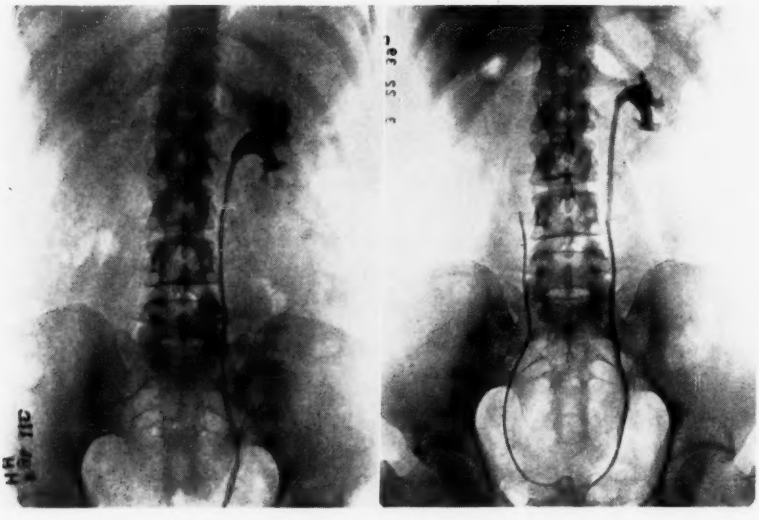
hydronephrosis may exist until advanced years of life and never be discovered unless superimposed infection occurs.

Although the diagnosis of an obstructive lesion complicating infection can be established finally only by complete urological investigation, including cystoscopy, ureteral catheterization, and pyelography (or intravenous urography in certain cases), some clue is frequently supplied by the clinical course and symptomatology.

To paraphrase the three R's of school days we may epitomize the three P's of obstructive infection in the urinary tract, which are *pain*, *pyrexia*, and *persistent pyuria*.

If we consider first only the supravesical lesions, the one outstanding differential symptom is pain. In the ordinary uncomplicated pyelitis kidney pain is not an outstanding symptom while in the presence of obstruction pain is the rule. This may be of a dull, dragging, aching type or it may be acute, severe, and colicky, the degree as well as type depending upon the suddenness and completeness of the obstruction. An infected kidney which has some drainage gives rise to mild pain compared with the kidney which is suddenly and completely obstructed.

Likewise, the severity of the febrile reaction is dependent upon the same factors. The more chronic, incompletely obstructed infection may give rise to only mild elevations of temperature so the urinary tract



a. b.

FIGURE 1: Woman, age 49. Complaint: Backache, fatigue, and poor endurance. No urinary symptoms but pus cells were found in the urine secured by catheterization.
a. Pyelogram shows marked dilatation of the upper calix; a stone was present in this calix.
b. Postoperative pyelogram nine months following heminephrectomy.

FIGURE 2: Woman, age 48. Complaint: Burning on urination, frequency, urgency, and chills and fever. Urine loaded with pus. Pyelogram shows advanced chronic bilateral pyelonephritis. Note particularly dilatation of the calices on the right with constriction of the infundibulae.

should therefore be considered in any unexplained, prolonged, low grade fever. In contrast to this the acutely obstructed infection may produce astounding temperature elevations even up to 106° F. or higher and yet, as a rule, the degree of prostration may be minimal.

The majority of the supravesical lesions are of course unilateral and this very fact also tends to indicate the presence of obstruction. Localizing symptoms are rarely absent in infected hydronephrosis and, in fact, in the majority of unilateral obstructed infections.

Persistent pyuria, however, is perhaps the most reliable guide to indicate the presence of an obstruction complicating infection for there are

FIGURE 3: Man, age 31. Complaint: Severe attacks of pain in the left kidney region associated with nausea, vomiting, and chills and fever. Pyelogram shows normal right kidney; marked hydronephrosis with infection on the left side. Operation: Left nephrectomy with removal of a large pyonephrotic kidney. Obstruction was due to an aberrant artery at the ureteropelvic junction.

some cases in which neither pain nor fever is present. This is particularly true in certain of the congenital lesions in children and Campbell[1] reports finding anomalies in 41 per cent of children who were investigated for chronic pyuria. Regardless of age, however, as a clinical rule one may say that any urinary tract infection in which the urine is not clear within four weeks under medical management should be completely investigated to rule out an obstructive lesion. The same rule should be applied to recurrent infections.

Of the obstructive lesions of the upper urinary tract, one occasionally encounters an inflammatory stricture of the infundibulum of a single

FIGURE 4: Man, age 28. Complaint: Pain in the left kidney region and persistent pyuria. Ureteropyelogram shows true inflammatory stricture of the lower third of the ureter with dilatation of the ureter and kidney pelvis above.

calix of the kidney (Fig. 1). More commonly this involves either the upper or lower calix, although in rare instances it may involve only a middle calix. Very commonly these cases are associated with stone and the treatment of choice is heminephrectomy since it is quite impossible to correct the stenosis of the calix. Unless the dilated, infected calix is removed, infection is likely to persist and recurrent formation of the stone is the rule. Another type of obstruction somewhat akin to this exists in the patients with chronic pyelonephritis in whom cicatricial constrictions of the calices frequently develop (Fig. 2). This results in obstruction to the individual calices and these constitute exceedingly

FIGURE 5: Boy, age 10. Only complaint was pus in the urine with absolutely no urinary symptoms. Ureteropyelogram through a nephrostomy tube shows marked hydronephrosis, ureteral dilatation, and tortuosity, with congenital stricture at the ureterovesical junction. Following pyelostomy drainage, plastic operation was performed upon the lower end of the ureter with relief of symptoms.

difficult problems in treatment. They are almost invariably bilateral and therefore operation cannot be performed.

Of the obstructive lesions at the ureteropelvic junction, the commonest perhaps is an impacted stone but next in frequency are the congenital obstructive lesions in the ureteropelvic junction, particularly the strictures, angulations, and aberrant vessels (Fig. 3). Although pain may call attention to the existence of lesions of this type, here again they are more commonly brought to the attention of the physician by the advent of infection. Medical management cannot hope to clear up these lesions; they are distinctly surgical problems and the decision as to conservative

FIGURE 6: Boy, age 15. Persistent pyuria and renal rickets. Bilateral pyelogram shows marked bilateral hydronephrosis and hydro-ureter. Congenital obstruction at bladder neck.

plastic operation or nephrectomy depends upon the degree of kidney damage.

A word of caution should be inserted here regarding the investigation of these hydronephrotic kidneys. Because the obstruction predisposes to infection, ureteral catheterization and diagnostic pyelograms sometimes initiate infection so that these patients should be ready for operation when such investigations are carried out.

In the ureter, stone is the most common obstruction. A stone may pass without infection but all too commonly infection complicates the problem. Particularly in the manipulation of stones must one be on guard because so frequently these procedures inaugurate infection above the impacted stone.

The other obstructive lesions in the ureter include the true strictures and particularly the congenital strictures at the ureterovesical junction (Figs. 4 and 5). The latter cases most frequently occur in children and, as a general rule, persistent pyuria or recurrent acute urinary infection is the thing which brings these to attention.

Rarely does one see primary ureteral tumors which produce obstruction. There are a number of extra-ureteral lesions which may cause ureteral obstruction by external compression. First and foremost of these is pregnancy which constitutes in reality a physiological type of obstruction and yet, because of this, the upper urinary tract in pregnancy is especially prone to infection. This usually clears up promptly after delivery, although if the infection has been severe, it may persist for a considerable period of time. Although both kidneys may be affected in the pyelitis of pregnancy, the more troublesome cases are often associated with a severe unilateral infection. Most cases will respond favorably to the use of properly chosen urinary antiseptics in conjunction with knee chest exercises to allow the uterus to fall away from the ureters, thus promoting better drainage. It is my firm belief that instrumentation should be avoided in the treatment of these cases until it is demanded by the failure of more conservative methods.

Pelvic tumors, particularly fibroids and ovarian tumors, may in a similar fashion produce ureteral obstruction as may also the rare cases of retroperitoneal tumors.

In the urethra, of course, by far the most common obstructive lesion is prostatic hypertrophy and other obstructions of the bladder neck. In this, as in other infravesical obstructions, the infection may be limited to the bladder. This is aggravated by the frequent association of saccules and diverticula which result from the obstruction and may become infected and cause prolonged cystitis. It is virtually impossible to clear up a cystitis in the presence of bladder neck obstruction; therefore, surgical relief in these cases is demanded.

The congenital urethral valves constitute a lesion of unusual interest and are invariably seen in children. In the vast majority of these cases the obstruction has existed since birth and even during intra-uterine life. In all the cases I have seen there have been markedly dilated ureters and kidney pelves so that the entire urinary tract is one communicating cavity (Fig. 6). Chronicity characterizes infection in these cases and even after obstruction has been relieved pyuria frequently persists. However, here again this lesion may exist for a considerable period of time before being recognized. I recall particularly the instance of a patient who had had very little trouble until the age of 14 years, when an infection developed and persisted. Investigation showed the presence of a congenital enlargement of the verumontanum.

I should like to emphasize particularly the association of urethral stricture with obstinate urinary infection. We have on numerous occasions seen patients with recurrent chills and fever in whom a urethral stricture was found and relief by internal urethrotomy and subsequent dilatations proved to be prompt and gratifying.

Summary

Attention has again been drawn to the effect of obstructive lesions of the urinary tract upon infections. Their recognition constitutes an essential part of the intelligent treatment of urinary infections and yet they are commonly overlooked. It is hoped that this repetition of facts which are common knowledge to many will stimulate others to consider the possible presence of these lesions in the more resistant infections of the urinary tract.

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MULTIPLE HEMORRHAGIC TELANGIECTASIS WITH SPECIAL REFERENCE TO GASTROSCOPIC APPEARANCE

JOHN F. RENSHAW, M. D.

The gastroscopic appearance of gastric telangiectasis has not been described, and a review of the literature revealed apparently only one description of the post-mortem appearance[1].

The following case is reported because telangiectases of the gastric mucosa were observed gastroscopically and because the patient presented an occult anemia in which the gastroscopic examination was an important diagnostic procedure.

A white man, a sheetmetal worker 44 years of age, was first seen at the Clinic on January 9, 1939, complaining of weakness and lack of strength. The present illness had its onset in the autumn of 1927 when, over a period of a few weeks, he noticed progressive weakness, lack of strength, and increased sensitivity to cold. This episode lasted three or four months but after he consulted his family doctor, it was relieved by the use of iron for a short time. No examinations of the blood or stools were made. Following this he apparently felt well until 1932 when he had a recurrence of similar symptoms which again were relieved by the use of iron for a short period. About October, 1936, the patient had six teeth extracted without any unusual bleeding but following the extraction he felt tired, run down, and cold all the time. He consulted another doctor in November, 1936, at which time his erythrocyte count was reported to be 4,240,000 and the hemoglobin was 27 per cent. Repeated examinations of stools showed occult blood by the benzidine test. After the patient used liver extract and iron, the hemoglobin was reported to be 90 per cent two months later, but from November, 1936, to March, 1937, the stools were consistently found to contain varying degrees of occult blood. The patient could not remember that any of his stools had been black except while iron therapy was used. There had, however, been some bright red blood in the stools without rectal pain on at least one occasion in 1935 and again in January, 1937. In March, 1937, he was referred by his family doctor to a consultant at which time the significant physical findings were pale skin and mucous membranes, except the nasal mucous membrane which was red, and red spots on the tongue, lips, and buccal mucosa. The spots were not raised or tender. A sigmoidoscopic examination revealed a pale mucous membrane and internal hemorrhoids. Otherwise the physical examination gave normal findings. Roentgen examination of the gastrointestinal tract was reported to reveal: "A very small defect in the pylorus" more suggestive of spasm than organic change. The duodenum

was normal and the colon was negative except for "moderate dilatation of the lower sigmoid and rectum." A gastroscopic examination was also done at that time. The fundus and cardia were reported to be normal. There was "some gastritis" of the antrum but in general the visualization was not satisfactory and the examiner asked for a recheck examination.

Other laboratory procedures were reported by the consultant as follows: The level of the hemoglobin was 72 per cent, the erythrocyte count was 4,530,000, the white blood count was 8,350 with a normal differential count. The urine showed no abnormalities. The stools were black and were 4 plus positive for occult blood and bile. A gastric analysis revealed 92 units of free hydrochloric acid and 110 of total acid. The indirect van den Bergh reaction was positive but the direct reaction was negative. The icterus index was 10 units. The Wassermann reaction of the blood was negative.

The patient was advised as to diet and medication, which was chiefly extract of belladonna before meals and alkaline powders frequently between meals. He did not follow the management carefully and because his symptoms of fatigue and weakness persisted, he was referred to the Clinic.

The family history was negative for any bleeding or anemia. The general questionnaire and review of the systems was negative except for the following features: As a child he had many nosebleeds and at the time of our examination his nose would bleed easily. He had not noticed the red spots on the tongue and lips until 1936 although his tongue had been sore intermittently since 1927. He had been singularly free from gastro-intestinal or abdominal distress. The bowel habits were normal and laxatives were not used.

Physical examination at the Clinic revealed the patient to be well developed and nourished. The skin was pale. There were multiple, small red spots around the mouth and on the lips, being more abundant on the lower lip with several on the cheek and nose. The lesions were oval or irregularly circular; very few were linear or web-like. They were not tender but blanched on pressure. They were a brilliant, blood-red color. The eyes, including examination of the fundus, were normal, as were the ears. There was a marked deviation of the nasal septum to the right and the turbinates were pale. A few telangiectatic lesions were seen scattered over the septum, turbinates, and in the nasopharynx. The tonsils had been removed. The vocal cords were smooth and freely movable but diffusely reddened because of telangiectasia. There was no lymphadenopathy. The thyroid was the usual size and consistency. The chest was clear to percussion and auscultation, the heart borders were within normal limits, and the tones were of good quality. No murmurs were heard. The rhythm was regular at 60 beats per minute. The systolic

blood pressure was 140 mm. of mercury and the diastolic pressure was 90 mm. of mercury. There was no abdominal tenderness and no masses or organs were palpated. The genitalia were normal except for a non-tender small swelling in the left testicle or spermatic cord. Several years previously the patient had been hit in this region with a baseball. Digital examination of the rectum was negative and an anoscopic examination for six inches showed no telangiectasia or hemorrhoids. The neurological examination gave normal findings.

A blood study by the special blood laboratory revealed an erythrocyte count of 6,260,000 cells with severe anisocytosis, poikilocytosis, and pallor. The hemoglobin was 11 grams per 100 cc. or 71 per cent. The volume of packed cells was 40 cc. per 100 cc. of blood, or 89 per cent. The volume index was 0.71, the color index 0.57, and the saturation index 0.80. The white blood cells numbered 4,250 and the differential count showed 55 per cent neutrophils, 31 per cent lymphocytes, 3 per cent eosinophils, 7 per cent monocytes, and 4 per cent basophils. There were no abnormal forms. The icterus index was 4 units and the platelets were normal. The mean cell diameter was 8.1 microns.

Other laboratory tests included examination of the urine which was normal. The blood Wassermann and Kahn tests gave negative reactions. The level of the fasting blood sugar was 104 mg. per 100 cc. Four liquid stools obtained following the administration of magnesium sulfate were examined while fresh on a warm microscopic stage and were found to be negative for ova or parasites but gave 2 and 3 plus reactions to benzidine. The fractional gastric analysis, using 35 grams of bread and 350 cc. of water, revealed the following acid figures at 15 minute intervals. No fasting secretion was obtained. Free hydrochloric acid was 20, 50, 60, 70, 60, 50, 30, and 40 units. The total acidity was 50, 90, 100, 90, 80, 80, 50, 60. There was no occult blood, mucus, or bile, and no food residue after 90 minutes. A duodenal drainage was normal.

The gastroscopic examination was easy and all parts of the stomach were well visualized, including the lesser curvature of the antrum. Cooperation was excellent. Peristalsis was unusually vigorous and deep, rolling out the entire antrum before reaching the pylorus. The pylorus in the patent phase was round and smooth; when completely closed there was considerable redundancy and puckering of the mucosa with regurgitation of the duodenal contents. The mucosa of the antrum was smooth, glistening, and orange-red. It appeared to be the usual color and texture. There were eight millet seed to pinhead sized, bright red spots in the mucosa (this is the actual size seen through the gastroscope and not the estimated size of the lesion in the stomach). These spots were circular and seemed to catch the highlight as if slightly raised.

They were all of uniform color, being a brilliant blood-red or carmine. The angulus was smooth and two more similar red lesions were seen on it. The musculus sphincter antri was high and smooth and there was one red spot on the crest of the fold (Fig. 1). In the lesser curvature of the body four additional such red spots were seen. The mucosa of the lesser curvature was smooth, glistening, and the usual pink to orange-red color. Just proximal to the level of the angulus, the mucosa of both the

FIGURE 1: Telangiectatic lesions on musculus sphincter antri of anterior wall.

anterior and posterior walls became lusterless and granular. The changes were progressively more severe in the upper parts of the stomach and in the upper half the mucosa was definitely granular and nodular. In some places, particularly on the posterior wall, it caused the mucosa to have a cobblestone or mosaic pattern. The folds, however, seemed to be of the usual caliber and distribution. Six more red spots were observed in the upper parts of the stomach but they were more widely scattered than in the lower part.

Diagnosis: 1. Hypertrophic gastritis of the body and fundus.
2. Multiple telangiectasia of the stomach.

COMMENT

The question of interpretation of these red lesions is important. How can we say that these are telangiectases rather than pigment spots or chronic localized gastric purpura? The lesions were considered to be telangiectatic because:

1. They were more widespread than pigment spots usually are.
2. The lesser curvature, where pigment spots usually occur more

abundantly than in any other region, was not involved any more than other areas of the stomach.

3. The lesions were all of a uniform, bright red color and showed no evidence of dark red or brown coloration commonly seen with older pigment spots. It is unlikely that so many lesions so widely separated should occur simultaneously.

4. The demonstration of telangiectatic lesions on the lips, tongue, buccal mucosa, nasal mucosa, nasopharynx, and vocal cords makes it seem reasonable that they could occur on the mucous membrane of the stomach.

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THE CLINICAL SIGNIFICANCE OF A LUMP IN THE BREAST

GEORGE CRILE, JR., M.D.

The final diagnoses in 200 consecutive cases of diseases of the breast seen at the Cleveland Clinic between June, 1935, and June, 1937, are shown in Table I.

TABLE I

200 Consecutive Diagnoses of Diseases of the Breast

Cystic disease	86
Chronic cystic mastitis	59
Cyst	23
Involutional disease	4
Total cystic disease	86
Carcinoma (one case in male)	69
Adenofibroma	19
Intraductal papilloma	6
Hypertrophy	6
Lipoma	4
Abscess	3
Benign hypertrophy — male	2
Paget's Disease, early (?)	1
Fat necrosis	1
Adiposis	1
Hematoma	1
Mastalgia	1
Total	200

One hundred forty-three of these 200 patients complained that they had felt a lump in the breast and in 43 per cent of these 143 patients, the lump proved to be carcinoma. Thus, regardless of age, nearly one-half the patients who complained of a lump in the breast were found to have carcinoma. A history of a lump in the breast can never be disregarded without a thorough investigation.

AGE

The age of the patient (Table II) is one of the most important factors in formulating one's judgment of the nature of a breast lesion and the indications for its treatment. Only 12 per cent of the patients with benign disease of the breast were over 50 years of age, whereas 75 per cent of the patients with carcinoma of the breast were more than 50.

TABLE II

Incidence of Benign and Malignant Disease of the Breast According to Age

Age	*131 Patients with Benign Diseases of Breast*	*69 Patients with Carcinoma of Breast*
Over 50 years	12.21%	75.36%
Over 60 years	4.58%	37.68%
Over 70 years	0	13.04%

Benign lesions in patients beyond 60 years of age were:

Duct papilloma	2
Involutional disease of the breast	1
Calcified adenofibroma	1
Fat necrosis	1
Benign hypertrophy in the male	1

From this table, it is apparent that benign lesions of the breast occur relatively rarely after the age of 50 years. Carcinoma, however, is not an uncommon finding in women from 40 to 50 years of age, 20 per cent of the carcinomas in this series having occurred in women in the forties.

Benign tumors of the breast, especially cysts, are also common in this age group.

In a group of 34 women between the ages of 40 and 50 in whom a definite mass was found in the breast, this mass was proved to be malignant in 41 per cent of the cases. It is therefore clear that, from a diagnostic standpoint, tumors of the breast present the greatest difficulties in women between the ages of 40 and 50. Beyond the age of 50, the chances are greater than 3 to 1 that the tumor is malignant. Under the age of 40 the chances are nearly 20 to 1 that the tumor is benign. But in the forties there is an almost even chance that the tumor is malignant and the history and clinical signs must act as guides to our decision.

SYMPTOMS

Except in rare instances the history is not of great value in differentiating benign from malignant lesions of the breast (Table III). It is true that pain or tenderness, especially when it is bilateral, is most apt to be the result of benign cystic disease. However, since more than one-fourth of the patients with carcinoma complained of some degree of pain or tenderness, the presence of these symptoms does not in any sense rule out carcinoma.

In this series, discharge from the nipple was associated with benign lesions more frequently than with malignant (8 to 5), but the presence of this sign must always arouse the suspicion of carcinoma.

TABLE III

Comparison of Symptoms Experienced by 131 Patients with Benign Lesions of the Breast and Those of 69 Patients with Carcinoma of the Breast

Symptoms	*131 Benign Lesions of Breast Per Cent*	*69 Carcinomas of Breast Per Cent*
Lump	62	90
Pain or tenderness	46	26
Discharge	6	7
No symptoms (lump discovered in course of routine examination)	5	0
Symptoms referable to distant metastases	0	12
Symptoms referable to axillary metastases, no breast tumor having been noted by patient	0	6

PHYSICAL FINDINGS

The presence of dimpling of the skin overlying the tumor or of fixation of the tumor mass to the chest wall is almost pathognomonic of carcinoma. In no instance were these signs associated with a benign tumor.

TABLE IV

Physical Signs

Signs	*131 Benign Tumors of Breast Per Cent*	*69 Carcinomas of Breast Per Cent*
Dimpling of skin or fixation of tumor to skin or underlying tissues	0	72
Axillary glands enlarged	1	50
Retraction of nipple without other evidence of fixation	3	4
Mass located in upper outer quadrant of breast	50	50
Average size of mass (estimated from examination)	2.1 cm.	3.7 cm.

Although the average size of the carcinomas in this series was greater than that of the benign tumors, there were several cases in which axillary metastases called attention to the breast as the site of a carcinoma so small that it could not be palpated.

Similarly, the presence of enlarged axillary nodes is reliable evidence in favor of the presence of carcinoma. Retraction of the nipple, on the other hand, is not necessarily indicative of carcinoma unless other signs of malignancy, i.e., puckering of the skin or fixation to the underlying structures, are present. In this series, there were only three cases of carcinoma of the breast in which the nipple was retracted in the absence of other signs denoting malignancy and in this same series there were four cases of benign tumors of the breast in which the nipple was retracted. In two of these cases, the lesions were cysts located beneath the nipple, in one a duct papilloma, and in the other a benign hypertrophy of the male breast. Any expanding tumor located beneath the nipple is capable of displacing the lactiferous ducts and thereby retracting the nipple. The diagnosis of carcinoma should, therefore, be made with some reservations in cases in which retraction of the nipple is the only sign indicative of malignancy.

Diagnosis

It is clear from a study of the foregoing data that carcinoma is the most common cause of a lump in the breast (1) in patients beyond the age of 50; (2) in the presence of dimpling of the overlying skin; and (3) in the presence of palpably enlarged axillary nodes. All other data deduced from the history or physical examination are of minor importance as compared to these findings.

In this series, the accuracy of the preoperative differential diagnosis between benign and malignant conditions was 96.5 per cent. In 2 of the 69 cases of carcinoma, an initial diagnosis of benign tumor was made. In one case the patient was 32 years of age and in the other 48. In neither case were the axillary glands palpable and there was no fixation of the tumor, retraction of the nipple, or dimpling of the overlying skin. A radical operation was performed as soon as gross examination of the specimen revealed its true nature.

In five of the 131 cases of benign lesions of the breast, the initial diagnosis was carcinoma. Three of the five patients were over 60 years of age and one patient (a man) had definite retraction of the nipple associated with benign hypertrophy of the breast. In the fifth case a detailed description of the lesion is lacking, a diagnosis of carcinoma having been made in the case of a periductal adenofibroma which was later shown to be benign.

In 10 per cent of the 69 cases of carcinoma, the diagnosis of malig-

nancy could not be made with sufficient certainty to warrant a radical mastectomy without more definite information as to the true nature of the tumor. In these cases a local excision of the quadrant of the breast containing the tumor was performed and after confirmation of the diagnosis of malignancy, the operator proceeded at once to do a radical mastectomy.

Differential Diagnosis of Benign Lesions of the Breast

The differential diagnosis of benign lesions of the breast is not of as much importance as the differentiation of benign from malignant lesions. It is always, however, satisfactory to both physician and patient when the pathological report is in exact accord with the clinical diagnosis.

Cystic Disease of the Breast

The most common benign lesion of the breast is cystic disease. This may assume the form of diffuse "chronic cystic mastitis" involving the entire breast and making it of a lumpy consistency, or there may be one or more discrete cysts. If superficial, these cysts may feel fluctuant, but more often than not they are tense and covered with sufficient breast tissue to make the recognition of fluctuation impossible.

The ages of the 86 patients with cystic disease of the breast varied from 22 to 66, 79 per cent of the 86 patients being between the ages of 30 and 50. Therefore it is in the involutional period of women's active menstrual life that cystic disease of the breast is most commonly seen.

If breast tumors are multiple or if they give a considerable amount of pain, it is quite likely that they are cysts. Sixty-four per cent of the 86 patients with cystic disease of the breast complained of having felt a lump in the breast. Pain or tenderness was experienced by 53 per cent of these patients and in 5 per cent a discharge from the nipple had been noted.

Periductal Adenofibroma

Periductal adenofibroma is the second most common benign lesion of the breast, this diagnosis having been made in 19 (15 per cent) of the 131 cases of benign diseases of the breast. In 79 per cent of the cases of adenofibroma, the patient complained of a lump; in 26 per cent, pain or tenderness had been noticed; in one case* (Fig. 1), the enormous size of the breasts was the chief complaint; and in three cases details of the history are not available.

Sixty-three per cent of the 19 cases of adenofibromas were in women under 35 years of age, the youngest being 13 and the oldest 66 years. Thus it is evident that adenofibroma is most apt to occur in women under 35 years of age and is as a rule painless and single, whereas breast

*Case report pending publication.

cysts are most common in women from 35 to 50, are more apt to be multiple, and to cause pain.

Papilloma of the Duct

The average age of the six patients with papillomas of the duct was 55 years, the youngest being 28 and the oldest 73. Five of these six patients complained of a lump in the breast, 3 complained of discharge from the nipple (bloody in one case), and one complained of pain.

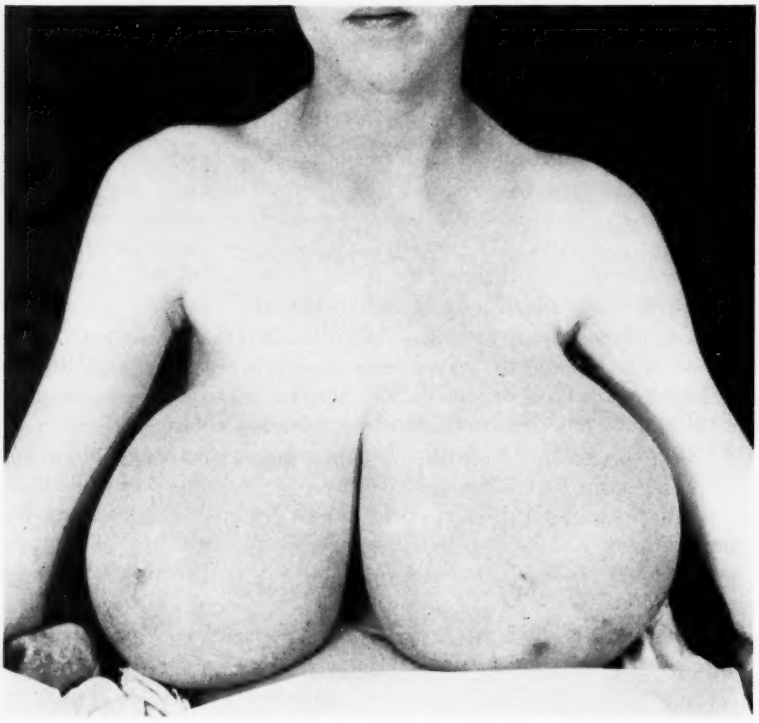

FIGURE 1: Enormous bilateral adenofibroma of breast in a girl 13 years of age.

Although 50 per cent of the patients with duct papillomas had noted discharge from the nipple, the relative infrequency of this condition makes it rank equally with carcinoma and cystic disease as the cause of discharging nipples.

Diagnosis and Treatment of Breast Tumors in Young Women

From the foregoing data, it is clear that the age of the patient is an important factor in the differential diagnosis of the various benign

lesions of the breast. The incidence of the various lesions in this series is indicated in the accompanying table (Table V).

TABLE V

Common Diseases of the Breast Tabulated by Decades

Diagnosis	*Number of Patients Under 30 Years of Age*	*Number of Patients 30 to 40 Years of Age*	*Number of Patients 40 to 50 Years of Age*	*Number of Patients Over 50 Years of Age*
Cystic disease	12	38	30	6
Adenofibroma	7	7	3	2
Papilloma of duct	1	0	0	5
Carcinoma	0	3	14	52

A definite lump was palpable in only eight of the 12 cases of cystic disease occurring in women under 30 years of age. In all seven cases of adenofibroma in this age group, a mass was palpable. Carcinoma is extremely rare at this age and duct papilloma is also uncommon. It can therefore be stated that a lump in the breast of a woman under 30 years of age has about an even chance of being an adenofibroma or a cyst. If nothing is found on examination to lead one to suspect malignancy, there is no contraindication to inserting a needle into the tumor and aspirating the contents. In about one-half the cases, according to Adair[1], this will result in the permanent disappearance of the cyst. If no fluid is obtained, however, the tumor should be excised and examined microscopically to ascertain that malignancy is not present. When a diagnosis of benign tumor of the breast is made in an older woman, carcinoma is always a possibility. The patient should therefore be prepared for a radical mastectomy and the tumor of the breast should be excised along with a generous surrounding margin of healthy breast tissue. If examination shows carcinoma to be present, the surgeon should proceed at once to remove the breast and the axillary contents.

HYPERTROPHY OF THE BREAST

One of the least serious but most troublesome lesions of the breast is the so-called benign hypertrophy. This condition usually occurs in young women, either married or single, and is characterized by the development of huge pendulous breasts that embarrass the patient because of their appearance and cause a great deal of discomfort because of their size and weight (Fig. 2). Although the etiology of this condition is not understood, it is possible that it is the result of an endocrine disturbance.

A number of plastic operations for the correction of pendulous breasts have been devised, but it is not recommended that surgery be applied

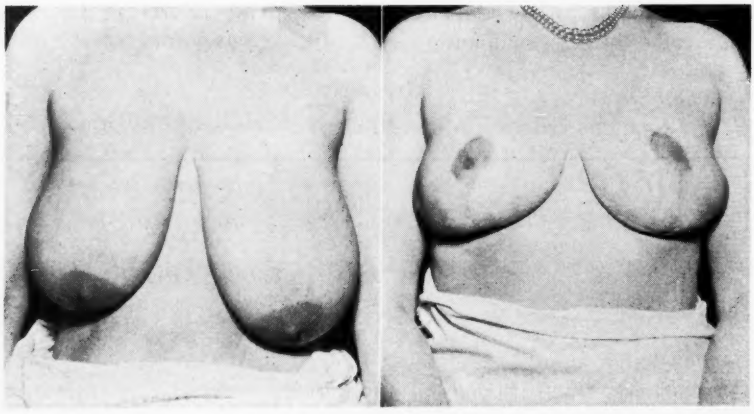

FIGURE 2A: Hypertrophy of breasts before operation.

FIGURE 2B: Same patient after plastic repair of hypertrophied breasts.

to the correction of the normal pendulous breast seen in women who have borne children. Surgery should be resorted to only in the correction of the deformity induced by a true benign hypertrophy of the breast. The type of patient who wishes a normal pendulous breast to be corrected by surgery will never be satisfied unless perfectly symmetrical virginal breasts are obtained whereas the patient with a true hypertrophy of the breast will be well satisfied to be relieved of the weight and encumbrance of the mass of superfluous tissue.

Successful results in the plastic repair of hypertrophied breasts have been consistently obtained by the technic of Fomon.[2] The operation consists of a hemimastectomy with removal of the lateral half of the breast, the nipple remaining attached to the medial half. The circulation to the medial half of the breast is not disturbed, the nipple is transplanted upward to a button hole in the skin made at the desired level, and the medial half of the breast is curled on itself in such a way as to reform the normal shape of the breast. The end result of such an operation is shown in figure 3.

RELATIONSHIP OF BREAST DISEASE TO THE ENDOCRINE SYSTEM

Much investigation of the endocrine relationships of benign lesions of the breast has been carried out by numerous workers. Geschickter, Lewis and Hartman[3] have gone so far as to state that a localized response of the breast to an endocrine disturbance produces fibro-adenomata; a generalized response of the breast to a similar disturbance results in virginal hypertrophy of the breast; and that an incomplete phase of epithelial development, again presumably dependent on an endocrine imbalance, causes chronic cystic mastitis.

In summarizing the relationship of the breast to the glands of internal secretion, all that can be said is that the growth and development of the normal breast is controlled by the endocrine system, and especially by the estrogenic hormones of the ovary. There has been much speculation as to the relationship of the painful breast, chronic cystic mastatitis, and adenofibromas to endocrine disturbances, but there is no convincing evidence that such a relationship actually exists. Endocrine therapy is often of value in treatment. The administration of estrogenic substances in doses of 5000 rat units once or twice a week will relieve the pain in many cases of cystic mastitis and mastalgia. The mechanism of this action is uncertain but it is probable that it lessens the congestion and edema, perhaps through inhibition of the pituitary. It is interesting to note that the administration of the male sex hormone, androsterone, has produced the same relief of pain.

It is not surprising that investigators have failed to demonstrate any consistent changes in the output of the various sex hormones in these cases. Our tests are still crude and depend upon assays made by injecting specimens of blood or urine into experimental animals. The response of the breast itself is certainly very sensitive to the hormones, and the breast is moreover constantly exposed to the action of the hormones of the body. It is more than likely that changes in endocrine activity too small to detect by laboratory means could result in changes in the breast leading to the production of pain, fibro-adenomas, or chronic cystic mastitis. The further investigation of this subject will depend on the development of more sensitive and more complete methods of endocrine assay.

Conclusions

1. A tumor of the breast in a woman from 40 to 50 years of age is almost equally apt to be either benign or malignant.

2. The history is not of much aid in the differential diagnosis of lesions of the breast. Pain or discharge from the nipple may be associated with either benign or malignant tumors.

3. Puckering of the skin is the most valuable early sign of carcinoma of the breast. Later, axillary metastases may aid in making the diagnosis.

4. Retraction of the nipple in the absence of other signs indicative of carcinoma cannot be relied upon as an index of malignancy.

5. Cystic disease of the breast is the most common disease producing a benign tumor of the breast. It is most frequently seen in women from 35 to 50 years of age, often tends to form multiple nodules, and commonly causes pain.

6. Adenofibromas most commonly occur in women under 35 years

of age, tend to be single, and to produce less pain than cysts of the breast.

7. Duct papillomas are usually seen in women beyond 50 years of age, and in 50 per cent of the cases cause a discharge from the nipple.

8. There is no contraindication to aspiration of cysts of the breasts in young women. In older patients, the tumor should be removed with a wide margin of breast tissue and radical mastectomy should be performed at once if carcinoma is found to be present.

9. Satisfactory cosmetic results can be obtained by plastic operations on hypertrophied breasts. It is urged that this operation be resorted to only in extreme cases.

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TOXIC AMBLYOPIA

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With the increased use of chemotherapy, it may be well to call attention to the symptom known to the eye physician as toxic amblyopia. Characterized by the patient as a veil, mist, fog, or haziness of the vision, further questioning reveals that this is in the direct vision and occurs most frequently in the morning. However, it is not uncommon for the cloudiness to increase during the day, usually affecting one eye, then the other, greatly alarming the patient as a rule. These cases comprise the acute group and if the condition is not recognized and appropriate measures instituted, a chronic amblyopia results. Patients in the latter group could be characterized as being apathetic—perhaps the visual fog includes the cerebrum.

References in the literature on this subject began in the middle of the eighteenth century. In 1751 an article by Boerhaave, as cited by deSchweinitz[1] appeared. In 1813 it was noted that drinkers of bitter beer had difficulty with their sight. For almost two centuries alcohol has been a primary factor in the production of toxic amblyopia.

deSchweinitz[1] in an excellent monograph published in 1896, lists some seventy-five drugs that have been known to produce this condition. The agent responsible for the amblyopia is usually designated in its name, such as alcohol amblyopia, tobacco amblyopia, etc.

Casey Wood[2] classified the drugs into two classes:

1. Poisons affecting the optic nerve
   a. Chronic retrobulbar neuritis.
   b. Poisoning producing other forms of optic nerve disease.
2. Poisons which cause symptoms of amblyopia but are unaccompanied by lesions in the retina or optic nerve.
   a. Agents producing mydriasis—dilated pupil.
   b. Agents producing miosis—contracted pupil.
   c. Agents producing irregular symptoms.

I believe that this classification, modified slightly by deSchweinitz, is the best available although it is evident that with our present knowledge of this symptom, no accurate classification is possible. It may be said that any drug can produce an amblyopia if the patient has an idiosyncrasy to that drug and if it is used over a period of time. The individual sensitivity is very important and must be taken into immediate consideration when any drugs are prescribed, whether they be given orally, intravenously, subcutaneously, by suppository, or by innunction. The absorption of the substance is all that is necessary to produce poisoning in certain individuals. The important point is that almost any drug can produce it and any reference to a cloudiness of vision

should be an indication for immediate discontinuance of all possible toxic substances, followed by a careful study to determine the causative agents.

The appearance of the fundus is as a rule normal. In rare instances edema of the macula may be seen, while in others there may be a questionable hazy disc. If the disease has become chronic, one is apt to find a definite greyish-yellow pallor of the inferior temporal portion of the disc which in most cases is rather indefinite. The nerve head in some instances has a "dirty color" with hazy margins and lacks sharp differentiation. It is not like the fairly sharp white or greyish-white seen in the retrobulbar neuritis of multiple sclerosis about which more discussion will be given later.

In every instance of toxic amblyopia, careful study of the eye is indicated as, associated with the loss of vision, there may be disturbances of the extra-ocular muscles, either as isolated paralysis or in nuclear groups. Diplopia is not uncommon. There are also pupillary changes as shown by the classification of Wood[2]. Some drugs dilate the pupil and others contract it. Changes in accommodation are frequently noted, especially in patients using atropine.

Undoubtedly, the most important sign is the change in the visual fields which is usually typical of the disease. First, the central field (foveal field) is as a rule involved—either a relative scotoma (loss that is not complete—a haziness) or an absolute scotoma in which no targets of any size are seen. These field losses may or may not extend to the normal blind spot (the optic nerve) and they may extend out to the periphery of the field. The study of the visual field is important and it is here that changes in the color field are of importance, as loss of red is seen very early in some cases. Progress studies of the fields are the only dependable way to study the results of treatment in this disease. Visual acuity is a second important factor, but without doubt the best sign is the patient's own statement that objects are more discernible and the mist is beginning to clear.

Careful history in regard to the patient's habits in obscure cases may elicit the causative agents. This requires extreme patience and tact as many people forget the fact that they are taking a cathartic daily and this may contain phenolphthalein; others, the self medicators, are not always willing to divulge their home remedies. Another group definitely hide the information, especially those who have been taking ergot or quinine. The mention of the fact that blindness may ensue unless all possible information is at hand is an excellent and truthful means of finding out the toxic agent. In the case of food poisoning, a rehearsal of previous meals may be necessary. All information is of importance and, in my experience, I have never had too much. In most instances,

it is only by sincere effort that sufficient knowledge is obtained.

Associated physical signs may contribute a great deal toward the diagnosis and determination of the etiological factor. A complete physical examination is indicated in all obscure cases and this may reveal the clue to the causative agent. A knowledge of any effect on the peripheral nerves, tissue changes, degenerations, and alterations in the blood, plus the effect on the special senses, such as hearing, are of value. Because the central vision is involved, no effort should be spared in the search for the causative agent. Hospitalization and repeated quizzing and examination are indicated if clues are not forthcoming.

There are a number of patients who suffer transitory loss of central vision. These individuals undoubtedly have toxic amblyopia. They use certain drugs very infrequently but in sufficient amounts to cause trouble occasionally; however, when they use the drug more regularly, a constant defect in the field may result.

A number of patients have noticed blurring of vision for a long period of time but, because the scotoma was unilateral and not always absolute, they did nothing about it; this is especially true of those patients who suffer with food allergy. Certainly this is true in almost all the cases in which optic atrophy is present. A few patients who have a sensitivity to foods, and probably the same may be said of plants, have had transitory loss of the central field with recovery following proper restriction of the diet. We have seen several patients who have had definite disturbances of the central field while taking vaccine for one reason or another. These patients are difficult to handle and care must be taken that the use of the vaccine be discontinued.

As one sees more of these patients, it becomes evident that any drug, food, or plant may affect an individual who has a sensitivity thereto and thus produce toxic amblyopia. Certain substances, since they are used by many people and have a definite toxicity, are therefore more common offenders than others. Good examples of these are tobacco, alcohol, quinine, and ergot.

Alcohol probably has held the attention of oculists for the longest period of time. The first report was that of drinkers of bitter beer who consumed large draughts of the substance at frequent intervals and in this manner were ingesting large doses of alcohol and possibly other products of fermentation. The drinker of poor alcoholic liquors is apt to be the patient with toxic amblyopia. It is possible, however, for the acute imbiber to have transitory amblyopia after a full night's drinking or a night's full drinking. Carroll[3] has shown that in many of these patients the alcohol is not the cause; rather it is a deficiency of vitamin B due either to inability of the patient to assimilate the vitamin or to a

lack of it. He has given some of these patients vitamin B but allowed them to continue their ingestion of alcohol and they have recovered. This is in keeping with the known action of vitamin B and might possibly be the explanation in some other forms of toxic amblyopia although, in my experience, patients with severe vitamin deficiencies have not shown field losses or visual losses as an outstanding feature of their deficiency.

There is the possibility that alcohol distilled from a grain to which a patient is sensitive might produce a greater reaction than another alcohol. A drinker of corn liquor may be sensitive to corn and not to alcohol. It is also known that poorly distilled alcohol contains too many and too much of the higher toxic alcohols. This is also true of the green or under-aged alcohols. The patients I have seen have mostly been drinkers of large amounts of alcohols over a long period of time although this has been associated with a definite lack of appetite and not infrequently with the use of tobacco.

Tobacco amblyopia presents itself more frequently than one is led to believe and probably will be seen even more often when women, who are notorious "chain-smokers," begin to suffer the effects of overindulgence. The worst cases of toxic amblyopia we have seen were in patients who chewed and smoked cigars or stogies—usually at the same time. It is well to remember that the heavy smoker never knows how much he smokes and he usually underestimates the amount. However, he generally carries an array of cigars in his coat pocket so that he will not run out in case of long delays anywhere.

Our worst cases of toxic amblyopia have been in patients who drank and smoked to excess; one man averaged between 25 and 30 stogies a day and these were soaked in corn liquor for flavoring. He also used a pint of liquor daily as well and to his credit it must be stated that he discontinued both and had almost complete recovery of vision. This occurred in spite of a very "dirty" disc and large field loss.

Chewing tobacco, cigars, and a pipe are the three worst offenders, but contrary to general belief cigarettes can produce toxic effects. Here again it is impossible to secure accurate information from the chronic smoker. By rough estimate three to four packages a day is the outside limit of possibility although a number of patients have used at least three packages. There are several potential dangers in cigarettes—the tobacco itself, toxicity in the paper, and substances used to flavor the tobacco. It is well to discontinue the use of alcohol and tobacco as soon as possible in patients having disturbances of vision. There is, of course, the possibility, as shown by Carroll, that the visual disturbance may be due to other factors. However, the irritating cause is still tobacco or alcohol and they, at the best, are of little value to the patient, radio, newspaper, and magazine advertising notwithstanding.

For treatment of tobacco and alcohol amblyopia, first discontinue the substances as much as possible. Give large amounts of vitamin B, especially in alcohol amblyopia, and increase the elimination from the body either by sweats or catharsis which must not be too drastic, and build the patient up with a diet high in vitamins. It is usually found that patients rarely have a deficiency in a single vitamin, especially if they have faulty dietary habits.

Under faulty dietary habits probably should be classified the individual who knowingly eats foods to which he is sensitive or who makes no effort to find out if transitory attacks of blurred vision need any treatment other than new lens. We have seen a number of patients whose visual complaint was due to food allergy and all the signs and symptoms of toxic amblyopia were corrected by restriction of the diet. Everyone is well aware of the acute toxic effect of certain foods on people with specific sensitivities. The same is possible over a long period of time when the sensitivity is to a food included in the daily or routine diet such as milk, coffee, wheat, or a fairly common offender such as chocolate.

Every patient who has a toxic amblyopia due to alcohol or tobacco should be thoroughly checked for other substances with which he comes in contact each day, as these are likely to be predisposing factors.

Certain individuals have been seen who have had specific sensitivity to substances where they worked; for example, a boy packing plants in moss in a commercial greenhouse had a severe unilateral amblyopia with a slight haze in the other eye. He had a cecocentral scotoma, a large blind spot by virtue of pure edema of the disc which looked like a hive of the nerve head. This was associated with loss of the central field. Removing him from that one location was all that was necessary to clear his sight. However, had he been allowed to continue in this work, I am certain that permanent changes would have taken place.

Toxic amblyopia is supposedly rare in women. This, I believe, is a statement not borne out by our present day experience. The women of today indulge in as much tobacco and in some instances as much alcohol as do the men. Several of our most acute and severe cases were in young women who had used ergot preparations in an attempt to correct failure to menstruate. In this type of case, the toxic effect is transitory. It may be necessary, however, to use sweats and elimination to shorten the period of toxicity to a minimum.

Another instance in a woman was when one individual, in an effort to cure a cold, took nearly a dozen cold tablets containing a salicylate and quinine. We used elimination and sweats as well as deep diathermy to the orbits. This patient responded slowly to treatment as

did a second woman with recurring headaches and a constant habit of taking empirin to relieve them.

It is more than likely that, if field studies were made in more instances, many more cases of toxic amblyopia would be found in women suffering from blurred vision. I am convinced that, in at least several of our patients with optic atrophy of unknown etiology, allergy was the cause as they were suffering with severe general allergy.

Two other substances which are commonly used and which have produced amblyopia are lead and arsenic. Lead is used in industry by painters and plumbers, and others use lead products to which they may be susceptible. A fairly large number of these cases have been reported in the literature.

Arsenic, whether given as a toxic agent or in one of the combination arsenicals used in the treatment of syphilis, has produced amblyopia in a number of instances and attention must be called to the toxic effects of some of the arsenic compounds on the optic nerve. Certainly some preparations are more toxic than others but there is a large factor of individual sensitivity which probably is as important to realize and know.

Mention must be made of the use of belladonna (atropine) and its derivatives. A very high percentage of people are sensitive to atropine and complain of visual disturbances. In most of these individuals, the eye disturbance is due to relaxation of the muscles of accommodation with pupillary dilation. In a few, however, the disturbance is in the macula or optic nerve and study of the field should be made, as in the latter group atropine should be discontinued, whereas a mild pupillary and accommodative disturbance is of no consequence.

Retrobulbar neuritis and toxic amblyopia have been used as synonyms. However, when one thinks of retrobulbar neuritis, one is apt to have in mind that change as seen in multiple sclerosis. The most bizarre, unusual, and untrustworthy fields are those in multiple sclerosis. Rarely are fields taken at intervals found to be the same and the fundus picture ranges from a severe neuritis to a normal nerve head.

The atrophy seen in multiple sclerosis is a white atrophic change and usually by the time atrophy has taken place other physical signs such as scanning speech and the loss of abdominal reflexes are present. Early cases of multiple sclerosis present a very definite problem in diagnosis, but every case of retrobulbar neuritis is not multiple sclerosis nor should every case of optic neuritis or retrobulbar neuritis be so classified without a thorough search for the etiological factor and a complete study for allergy.

Multiple sclerosis offers a poor prognosis whereas toxic amblyopia

may definitely be benefited by proper management. It is well to remember that in 50 per cent of all cases of multiple sclerosis there is involvement of the optic nerve in one form or another.

There is a condition classified as pseudo-sclerosis which simulates multiple sclerosis but which produces no changes within the eye at all.

No effort has been made to discuss the pathological processes underlying the loss of vision. It might be well to draw attention to the usual changes taking place. There is usually a cellular edema which is a transitory process in most instances. This, when chronic, is replaced by round cells or small lymphocytes and eventually by connective tissue which is the final stage of permanent loss or atrophy.

Summary

Toxic amblyopia might be classified in two types: (1) acute and (2) chronic. These two types can be further subdivided according to the action of the substance. In both types there is similar loss of vision. In the chronic type, there is usually atrophy.

Immediate withdrawal from or removal of the offending drug, food, or chemical is important. The treatment is more that of management, as further use of drugs may add to the difficulty during a severe stage of hypersensitivity.

Elimination and sweats are indicated. Deep diathermy to the orbits should be attempted.

Use of the eyes should be restricted.

The prognosis is good in most of the acute cases. In chronic cases with atrophy, more vision tends to be lost before the process is completely halted.

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